The Journal of the American Medical Profession

MEDICAL TIMES

Pulmonary Embolism
Multiple Sclerosis
Amebiasis
Laceration of Liver
General Practice

Medical Book News
Contemporary Progress
Editorials
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Vol. 77 March 1949 No. 3

a new antihistamine

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relief of pruritus

Thephorin, the new antihistamine with minimal side reactions, is now available in 5 percent ointment for effective relief of distressing allergic skin manifestations. In most cases Thephorin Ointment quickly relieves the discomfort of atopic dermatitis, chronic contact dermatitis, lichenified eczema, pruritus ani, pruritus vulvae, urticaria and drug dermatitis. 1½ oz. tubes and 1 lb. jars.

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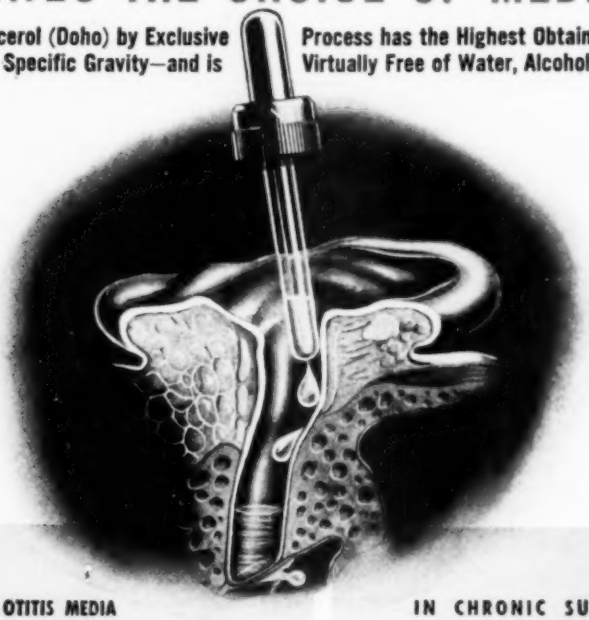

IN ACUTE OTITIS MEDIA

REMOVAL OF IMPACTED CERUMEN

AS AN ADJUNCT TO SYSTEMIC ANTI-INFECTIVE THERAPY, AS PENICILLIN, ETC.

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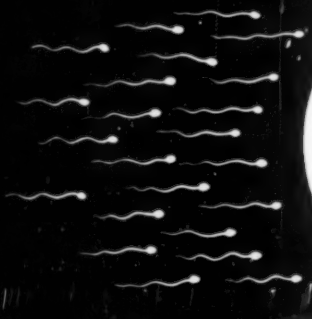
Simplicity



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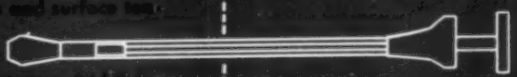

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whenever indicated—wherever prescribed

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Medical Book News

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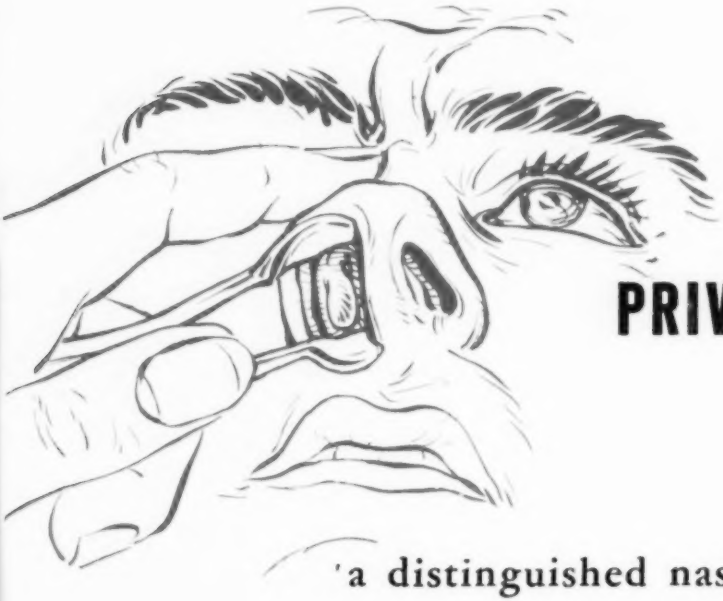
℞: only 2 or 3 drops



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complicating
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100
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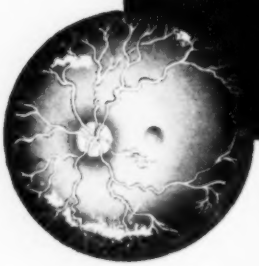
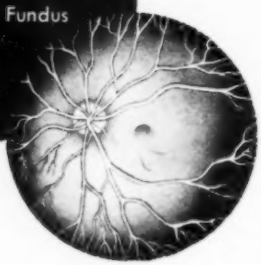
Ocular Fundus in Degenerative Vascular Disease—Hypertension, Diabetes, Arteriosclerosis —note tortuous blood vessels, areas of exudation, hemorrhagic areas.



Normal Ocular Fundus



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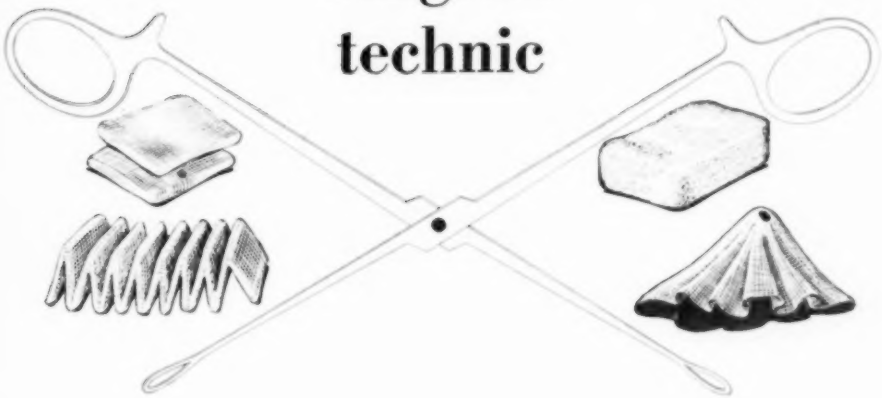

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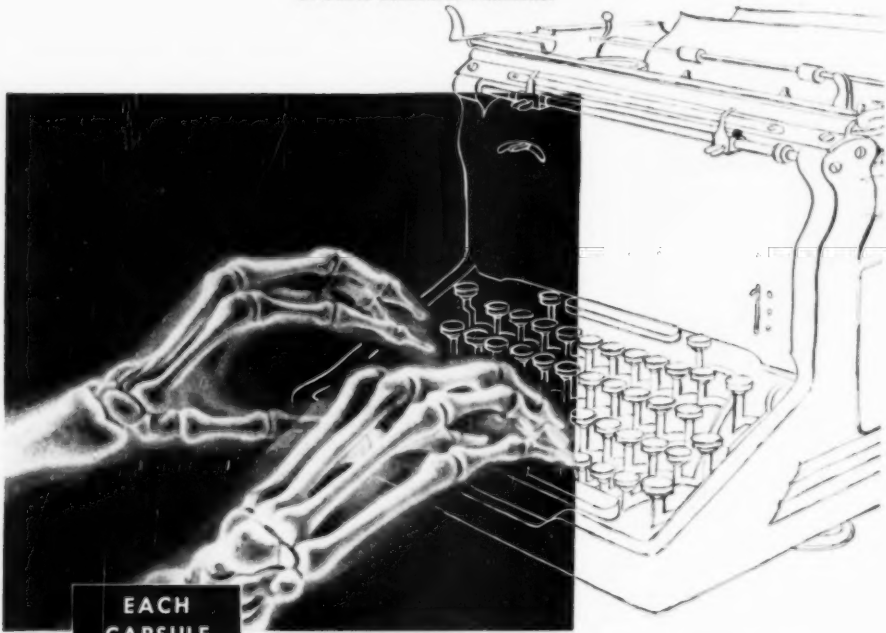

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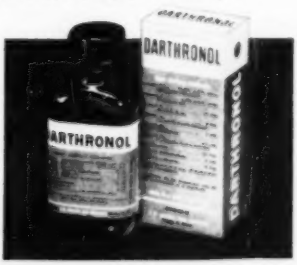

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100,000 units micro-pulverized penicillin G sodium.

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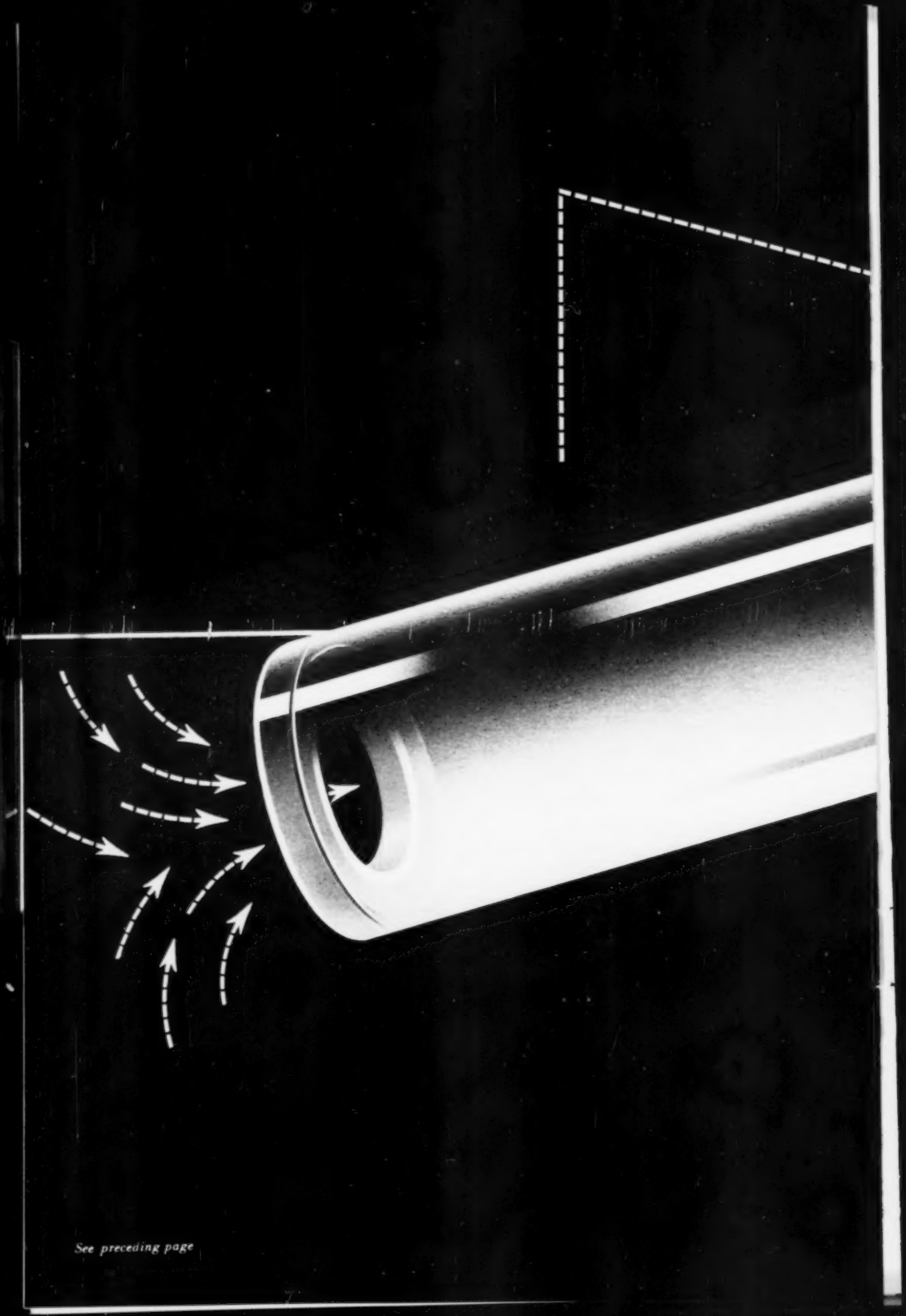

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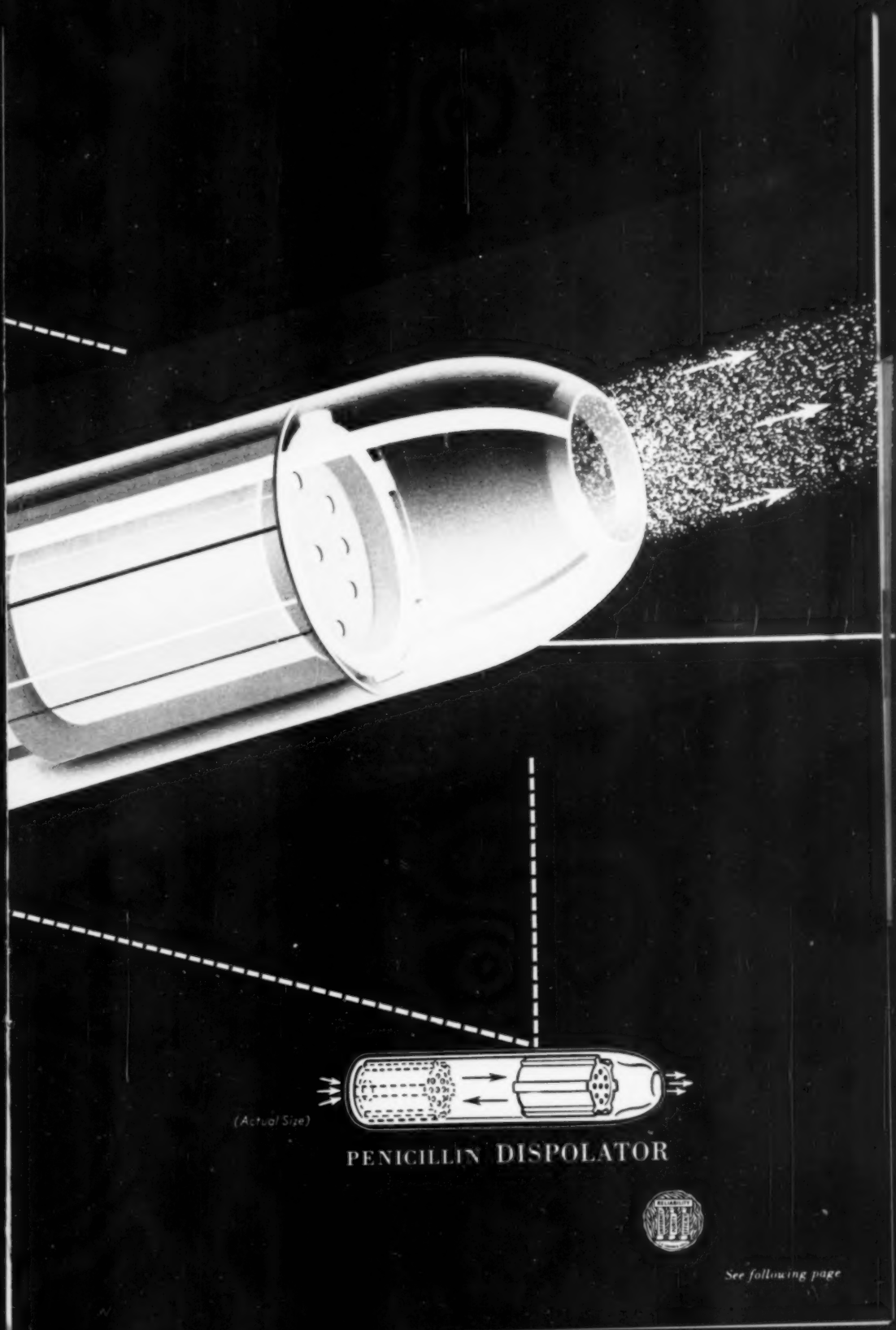
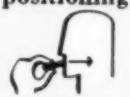
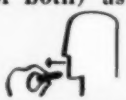


(Actual Size)

PENICILLIN DISPOLATOR

See following page

Penicillin Powder Inhalation Therapy with the Penicillin DISPOLATOR

100,000 units, micro-pulverized penicillin G sodium  is contained in a plastic cartridge  covered  with a plastic screen. This unit is enclosed in a plastic barrel open at both ends.  The penicillin-containing cartridge is held in place by a plastic positioning rod  so that penicillin will not spill out. ℞ When you prescribe the Penicillin Dispolator, to use, the patient merely removes the Dispolator from the sealed vial, takes out the positioning rod  and inhales through mouth or nostrils  (or both) as directed. After each inhalation, he removes the Dispolator  before exhaling and replaces it for the next inhalation, etc. (20 to 25 inhalations may be necessary to utilize the penicillin). Disposable  after the total dose is inhaled, the Dispolator is discarded. Supplied in Packages of 3.

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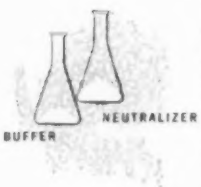

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PROGYNON PELLETS

PROGYNON

For intramuscular injection:—PROGYNON-B* (Estradiol Benzoate U.S.P. XIII), PROGYNON-DP* (Estradiol Dipropionate) and MICROPELLETS PROGYNON** (pure Estradiol U.S.P. XIII in aqueous suspension).

For oral use:—PROGYNON-DH* (Estradiol U.S.P. XIII) in tablets.

For topical application: — PROGYNON-DH in ointment, vaginal suppositories and nasal spray.

For implantation: — PROGYNON PELLETS (Estradiol U.S.P. XIII).

*®

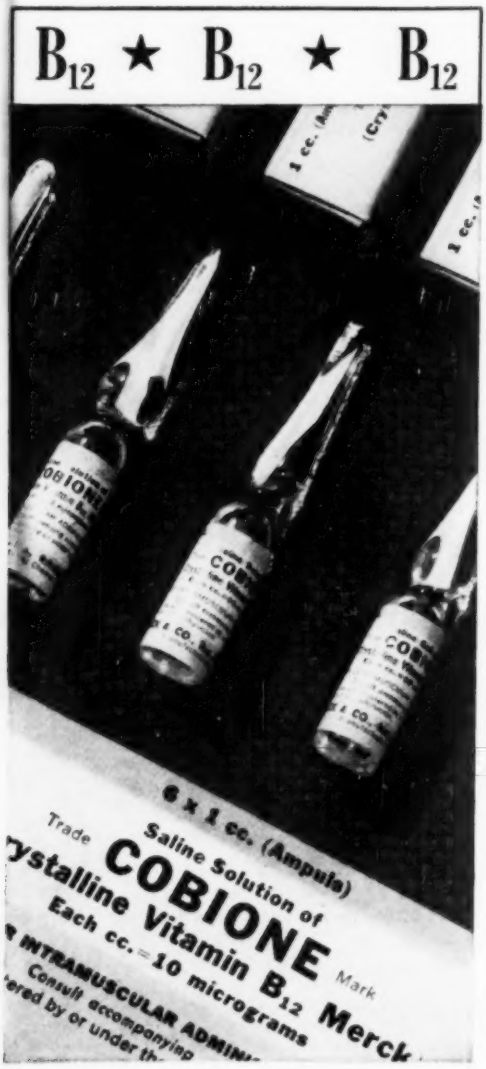
**MICROPELLETS PROGYNON trade-mark of Schering Corporation

Schering

CORPORATION · BLOOMFIELD, NEW JERSEY

IN CANADA, SCHERING CORPORATION LIMITED, MONTREAL

Now Available..



FIRST isolated in the Merck Research Laboratories in 1948, clinical studies have demonstrated that Cobione* exhibits extremely high hematopoietic activity in the following conditions:

★ **PERNICIOUS ANEMIA**
In uncomplicated cases and those with neurologic involvement.
In patients sensitive to liver preparations.

★ **NUTRITIONAL MACROCYTIC ANEMIA**

★ **CERTAIN CASES OF MACROCYTIC ANEMIA OF INFANCY**

★ **SPRUE** (tropical and nontropical)

Cobione* Possesses Significant Advantages

- It is a pure, crystalline compound of extremely high potency, and no known toxicity, when given in recommended dosage.
- It is effective against all manifestations of pernicious anemia, including the neurologic manifestations.
- It is effective in, and well tolerated by patients sensitive to all liver preparations.
- It is effective in extremely low doses, because of its remarkably high potency.
- It may be administered in precise dosage, because it is a pure, crystalline compound.

*Cobione is the trade mark of Merck & Co., Inc. for its brand of Crystalline Vitamin B_{12}.

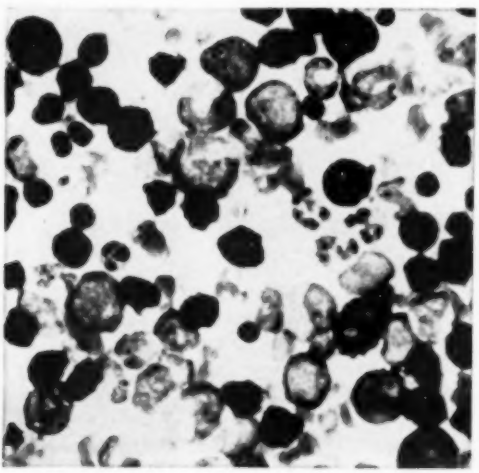
COBIONE

TRADE MARK

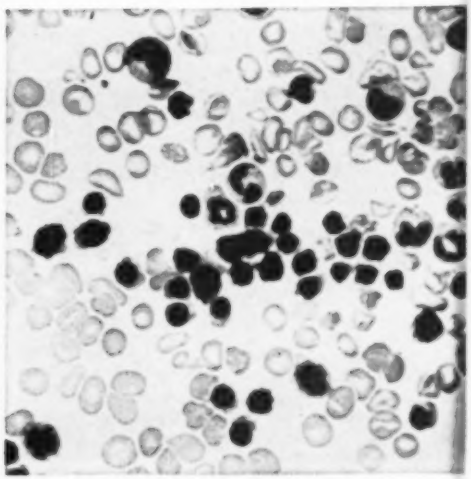
(CRYSTALLINE VITAMIN B_{12} MERCK)

★ ★ ★

Antipernicious Anemia Factor of Liver in Pure, Crystalline Form



Pernicious anemia before treatment with Cobione (Megaloblastic Bone Marrow)



Same patient ninety hours after a single injection of 0.025 mg. of Cobione

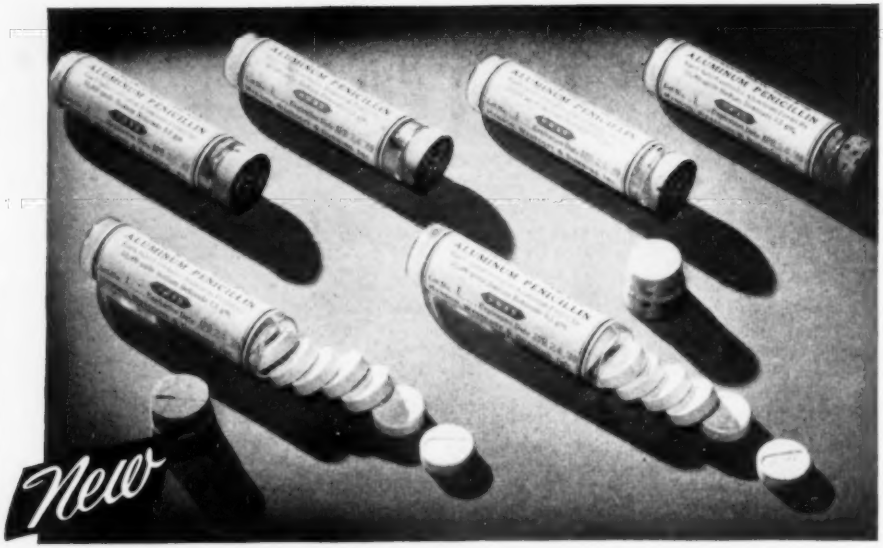
COBIONE

TRADE MARK

(CRYSTALLINE VITAMIN B_{12} MERCK)

MERCK

MERCK & CO., Inc. *Manufacturing Chemists* RAHWAY, N. J.



Aluminum PENICILLIN.*

ORAL TABLETS

Aluminum Penicillin Oral Tablets are clinically effective in the treatment of penicillin susceptible infections.

Containing the almost insoluble trivalent aluminum salt (not a mixture), they provide for maximum utilization of the dose administered.

Low solubility of Aluminum Penicillin renders it much less liable to inactivation in the stomach. Destruction in the intestinal tract is inhibited by the addition of sodium benzoate. Slow conversion to a readily absorbed form in the more alkaline conditions of the intestinal tract enhances clinical effectiveness.

Aluminum Penicillin is not toxic in doses far exceeding those used therapeutically and does not cause gastric disturbance.

Detailed information will be sent to physicians on request.

Specify Aluminum Penicillin Oral Tablets, H. W. & D.

Supplied in vials of twelve tablets each containing Aluminum Penicillin, 50,000 units, and sodium benzoate, 0.3 gram.

*Patent applied for

NOW COUNCIL ACCEPTED

Oral Tablets

HYNSON, WESTCOTT & DUNNING, INC. BALTIMORE MARYLAND

TO VITALIZE THE "Sickly" CHILD...

You know little fellows like this — never really well — always hypersusceptible to every infection and childhood disease. Their recovery from each illness is distressingly slow and leaves them listless, sluggish in appetite, dull of eye and sallow skinned. For such as these, prescribe:

INFAZYME

A Specialized Nutrient for Infants and Children providing

B COMPLEX · IRON · AMINO ACIDS

A CONCENTRATED RECUPERATIVE NUTRIENT specifically for children, providing supplementary amounts of the amino acids, readily available iron, and high potencies of the clinically important B vitamins complemented with the whole B complex as derived from liver, rice bran and hydrolyzed yeast.

The 30% yeast hydrolysate in Infazyme contains all ten essential amino acids, with polypeptides and other amino acids, in adequate amounts to stimulate vitamin assimilation and hemoglobin formation.[1,2] So, in addition to prodding a "lazy" appetite,[3] Infazyme facilitates more complete utilization of the child's food.

TASTE APPEAL —Infazyme has a rich fruity tang that is accepted eagerly by even the anoretic child. Typical liver, iron and amino acid tastes are successfully disguised. Usual dosage is 5 cc. (1 teaspoonful) three times a day, preferably in milk or fruit juice, before or with meals.

✓ *Check this unique FORMULA*

EACH 15 CC. CONTAINS:

Protein Hydrolysate (45% amino acids)	5.0 Gm.
Thiamine Hydrochloride	3.0 mg.
Riboflavin	2.0 mg.
Niacinamide	12.0 mg.
Pyridoxine Hydrochloride	1.0 mg.
Liver, B Complex Fraction	67.5 mg.
Rice Bran Extract	67.5 mg.
Peptonized Iron, N. F.	135.0 mg.

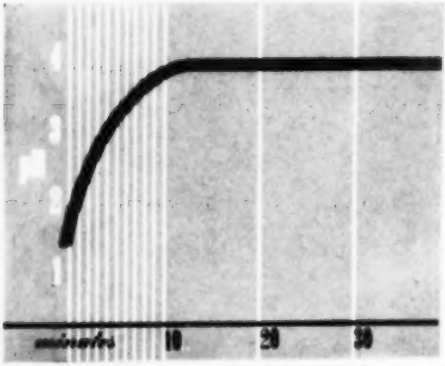
Available at prescription pharmacies and hospitals in 4-oz. and 12-oz. bottles

1. Ruskin, S. L.: The role of the coenzymes of the B complex vitamins and amino acids in muscle metabolism and balanced nutrition, Am. J. Dig. Dis. **13**:110-112 (1946).
2. Jacobson, M.: Preliminary report on the combined effects of vitamin B complex with amino acids, N. Y. State J. Med. **45**:2079-2080 (1945).
3. Summerfeldt, P. and Ross, J. R.: Value of an increased supply of vitamin B and iron in the diet of children, Am. J. Dis. Child. **56**:985-988 (1938).

Infazyme ®

MERRELL 1828

THE WM. S. MERRELL COMPANY · CINCINNATI, U. S. A.



Rapid and Prolonged RELIEF in Peptic Ulcer and Hyperacidity . . .

The present trend of treatment is to alleviate the underlying factors as well as the symptoms. Psychotherapy, rest and diet regulation are generally employed. Relief is achieved through acid buffering and sedation.

ALZINOX

Brand of

Dihydroxy Aluminum Aminoacetate

ALZINOX, a new and efficient antacid, was subjected to thorough biochemical and clinical investigations and proof of its effectiveness established. Case histories are on file and available upon request. The glycine buffer gives quick action; the aluminum in suspension gives *prolonged* buffering action. The "one-two-punch" action of ALZINOX is effective and safe; there is no danger of alkalosis or of acid rebound since the pH goes no higher than pH4.5 even when ALZINOX is given in excess. Hyperacidity is controlled within the safe range of pH4 to pH5.

ALZINOX is available in plain-uncoated tablets, each containing dihydroxy aluminum aminoacetate 0.5 Gm. (7.7 grs.) The suggested dosage is one or two tablets one to two hours after meals and upon retiring, or as directed by the physician. Supplied in bottles of 100 and 500.

ACCEPTED COUNCIL ON PHARMACY AND CHEMISTRY AMERICAN MEDICAL ASSOCIATION

THE E. L. PATCH COMPANY
BOSTON, MASS.

LETTERS

TO THE EDITOR

SUMMARY ARTICLES

"Thank you very much for your reprint of the article 'Angina Pectoris,' published recently in the MEDICAL TIMES. Often during my practice of over twenty years I have had the need and urge to bring my knowledge of a certain subject up to date, but like many other busy doctors could not find the time or inclination to wade through extensive literature. I have often wished that some editor would publish a symposium just as you are now doing to abstract the literature on a subject down to twenty or thirty pages of good reading and to incorporate in a short space all of the pertinent facts relating to the subject.

"You have probably had in your experience and I know I have had in mine the feeling that some articles are excellent but many are valueless and are a waste of time to read because they contribute no advance in thought or knowledge.

"I wish to congratulate you on your symposium idea because I think it constitutes a valuable piece of editorship."

Myron L. Hafer, M.D.
Patchogue, N. Y.

"Your summaries of an entire medical subject are most helpful. It is hoped that you will continue this type of reporting."

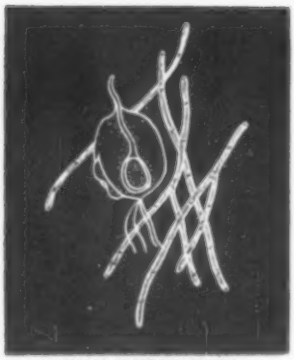
D. W. Davis, M.D.
Three Rivers, Texas

LIKE MT

"I like your magazine. The choice of the material is excellent. What the busy G.P. needs."

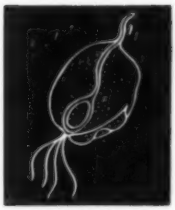
N. W. Nemiroff, M.D.
Oradell, N. J.

—Continued on page 46a



DUAL INFESTATION

MONILIA



TRICHOMONAS

specific for vaginal trichomoniasis

"All patients became symptom-free and bacteriologically negative..."[1]

now effective in moniliasis

"Symptomatic cure was effected in about 80% and mycologic cure in about 50%..."[2]

AVC (Allantomide Vaginal Cream) has long been accepted by clinicians as specific for the treatment of vaginal trichomoniasis. Investigators have unanimously reported it effective in 98-100% of cases.

With the addition of 9-aminoacridine, a new, potent antiseptic agent, AVC IMPROVED is capable of effecting mycologic cure in moniliasis.[2] Thus, AVC IMPROVED may be expected to provide relief in those stubborn cases of vaginitis which are due to mixed infections.

Available in 4 oz. tubes, with or without plastic applicator.

1. *Horoschak, A., and Horoschak, S.: Jl. Med. Soc. N. J., 43:92, Mar., 1946.*
2. *Dill, L. V. & Martin, S. S.: Med. Ann. Dist. Col., 17:389, July, 1948.*

AVC IMPROVED

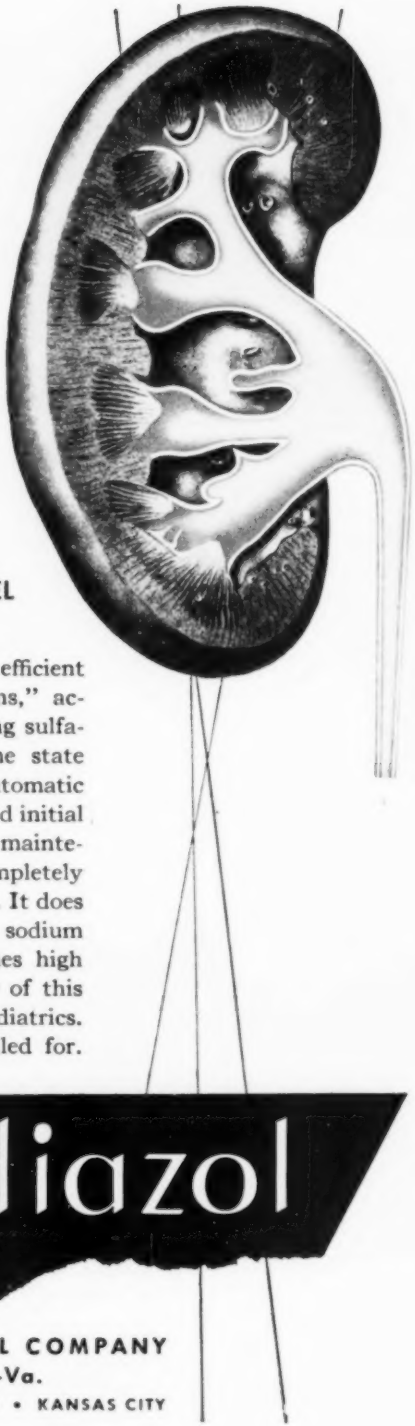
ALLANTOMIDE VAGINAL CREAM with 9-Aminoacridine

THE NATIONAL DRUG COMPANY, PHILADELPHIA 44, PA.

Manufacturers of

Pharmaceutical, Biological and Biochemical Products for the Medical Profession

A Higher Standard In Sulfonamide Therapy



REDUCED RENAL HAZARD
MORE RAPID INSTITUTION OF BLOOD LEVEL
AUTOMATIC ALKALIZATION

Use of sulfonamide mixtures, called "the most efficient single measure to minimize renal complications," accounts for the superiority of Aldiazol. Presenting sulfadiazine and sulfathiazole in a microcrystalline state together with sodiums citrate and lactate for automatic urinary alkalization, Aldiazol produces more rapid initial sulfonamide absorption, leads to satisfactory maintenance of therapeutic blood levels, and almost completely eliminates the danger of crystalluria (2 per cent). It does not burden the kidneys unnecessarily as does sodium bicarbonate alkalization. Aldiazol thus combines high efficacy with minimal toxicity. The palatability of this liquid preparation makes it especially useful in pediatrics. Indicated whenever sulfonamide therapy is called for.

SE MCO

Aldiazol

THE S. E. MASSENGILL COMPANY
Bristol, Tenn.-Va.
NEW YORK • SAN FRANCISCO • KANSAS CITY

A new measure for better cough control

'Elixoid'

"ELIXOID" Brand Cough Syrup contains:

Ethylmorphine Hydrochloride for its highly efficient action in suppressing unproductive cough. Given for grain, a more potent analgesic than codeine. Especially desirable where pain or night cough prevents sleep.

Sodium Citrate for its liquefying effect. Preferred over salts for its systemic alkalizing properties.

Citric Acid as a buffer, for stability and full potency.

Fluidextract of Ipecac in low, non-emetic dosage, to synergize the secretion of protective fluids.

Menthol for its cooling, soothing, analgesic effect on convoluted sore throat.

Aromatic Syrup, a delicious flavor to ensure acceptance by both children and adults—and just vivid enough to provide a local demulcent effect.

SAFETY: 'Elixoid' Cough Syrup is an exempt preparation under Federal Narcotic Law. (Consult state and local Acts for local status.)

DOSAGE: One teaspoonful in water every three hours or as directed. Children, according to age.

'Elixoid'

brand **COUGH SYRUP**

contains no alcohol, chloroform or barbiturates

BURROUGHS WELLCOME & CO. (U.S.A.) INC., TUCKAHOE 7, NEW YORK

protection for the unborn child

Romulus and Remus, the twins abandoned at birth, were nurtured and protected against the hazards of infancy by a she-wolf.

The unborn child may be assured of intrauterine nurture through protection against the hormone accidents of pregnancy—abortion, premature labor and toxemia—by **des,** Grant's triply crystallized **di**ethyl**s**tilbestrol in 25 mg. tablets.

In 1941 Karnaky[1] found high-dosage **di**ethyl**s**tilbestrol therapy to excel all previous methods—including the use of all progestins—against threatened and habitual abortion and premature labor.

Rationale for this therapy resulted from the work of Smith, Smith and Hurwitz[2], and Meaker[3] who showed **di**ethyl**s**tilbestrol to increase production and utilization of endogenous progesterone, thus protecting the pregnancy. These investigators concluded that 25 mg. oral tablets of **di**ethyl**s**tilbestrol were most effective protection against accidents of pregnancy referrable to progesterone deficiency — threatened and habitual abortion, premature delivery, pre-eclampsia and intrauterine death.

Rosenblum and Melinkoff[4] employed 25 mg. oral tablets of **di**ethyl**s**tilbestrol in treatment of a large group of cases of threatened and habitual abortion and of threatened premature labor "with more favorable results than . . . with any other type of treatment."

References: 1. Karnaky, K. J.: Original gynecological and obstetrical research—sterility, endocrine and vaginal operations. M. Rec. & Ann. 35:851, 1941. 2. Smith, O. W., Smith, G. van S., and Hurwitz, D.: Increased excretion of pregnanediol in pregnancy from diethylstilbestrol with special reference to the prevention of late pregnancy accidents. Am. J. Obst. & Gynec. 51:411, 1946. 3. Meaker, S. R.: A working classification of the causes of abortion. J.A.M.A. 123:680, 1943. 4. Rosenblum, G., and Melinkoff, E.: Preservation of the threatened pregnancy with particular references to the use of diethylstilbestrol. West. J. Surg. Obst. & Gynec. 55:597, 1947.

des
25 milligram tablets

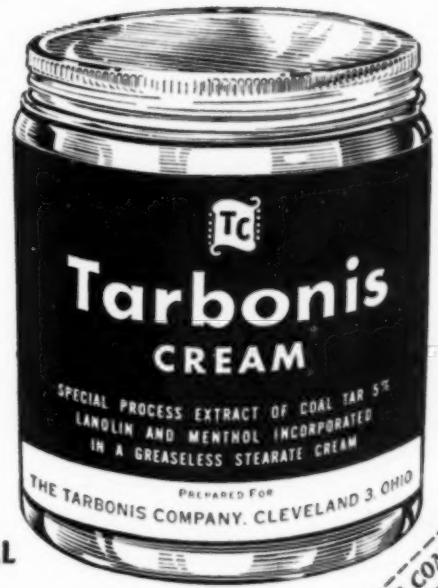
Available in containers of 100, 500, and 1,000 cross-scored tablets, 25 mg. at all pharmacies and from:

GRANT CHEMICAL COMPANY, INC., 95 MADISON AVE., NEW YORK 16, N. Y.

The Original

CLEAN WHITE COAL TAR CREAM

All the Therapeutic Advantages of Crude Coal Tar with Irritating Residues Removed



- **ECZEMAS**
- **PSORIASIS**
- **SEBORRHEIC DERMATITIS**
- **VARICOSE ULCERS**
- **OCCUPATIONAL DERMATITIS**

Where infection complicates the clinical picture* SUL-TARBONIS (TARBONIS *with 5% sulfathiazol) is recommended.

THE TARBONIS COMPANY, DEPT. MT
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Please send me a clinical sample of
TARBONIS ____, SUL-TARBONIS ____

M. D. _____

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CITY _____ ZONE _____ STATE _____

Simplified Control of

DIAPER DERMATITIS

Due to Ammoniacal Urine

METIONE

REG. U. S. PAT. OFF.

[METHIONINE]

GRANULATED

The results of over forty years of investigation establish that ammonia occurs in the urine as a product of internal metabolism.

*New clinical findings** demonstrate that METIONE† combats the development of ammoniacal urine, thus preventing or controlling napkin dermatitis due to this cause. The daily administration of 3 grains of methionine as provided in METIONE GRANULATED effected disappearance of ammoniacal urine within two to three days in 54 instances. When given prophylactically to 50 infants, no case of ammoniacal urine developed.

METIONE GRANULATED is designed especially for pediatric use. Dissolves quickly in milk . . . well tolerated.

(This product is not to be confused with METIONE Powder, which is flavored, and designed for use in adults.)

METIONE GRANULATED is supplied in bottles containing 30 Gm. (1 oz.). One level teaspoonful supplies 3 gr. (0.2 Gm.) of D,L – Methionine. Literature and samples will be sent to physicians on request.

*Goldstein, L. S.: Tuberculology, August, 1948.

†The word METIONE is a registered trademark.

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1841 BROADWAY NEW YORK 23, N. Y.

Marvin R. Thompson, Ph.D., through original laboratory methods has succeeded in the development of a unique lacto-salicylate compound which provides liquid salicylate therapy in the ultimate, at the same time by-passing untoward effects generally associated with acetosalicylic acid and other related salicylate administration.

power . . .
and speed without penalty in salicylate therapy!

SYRUP LACTO-SALICYLATE CO. -MRT

(An original MRT contribution)

SYRUP LACTO-SALICYLATE CO.-MRT is an exceptionally stable and palatable syrup containing sodium salts of salicylic and lactic acids.

INDICATIONS: Recommended for use whenever aspirin or other salicylates are indicated; namely as an analgesic and antipyretic agency in colds, grippe, rheumatic disease, gout, neuralgias, arthritis, etc.

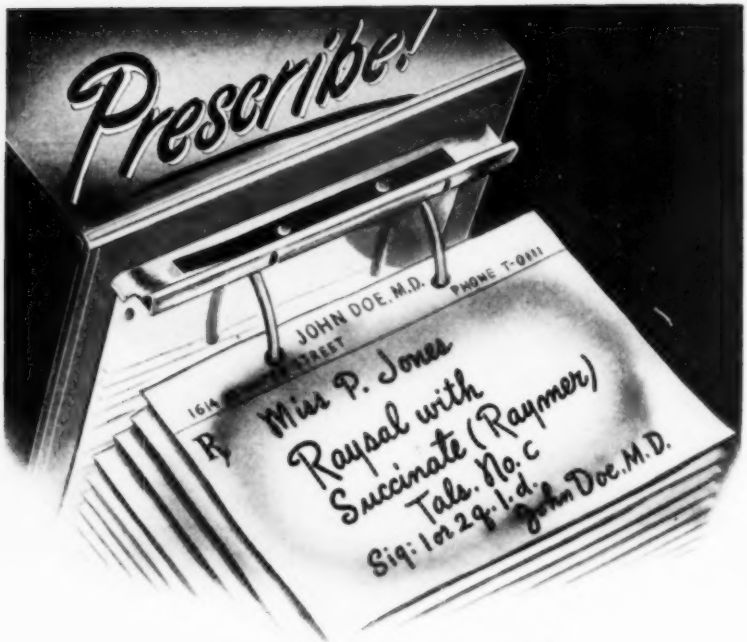
Each teaspoonful (5 c.c.) of SYRUP LACTO-SALICYLATE CO.-MRT contains 1.5 Gm. of sodium lactate and 0.3 Gm. of sodium salicylate representing the full potency of 5 grains of acetosalicylic acid (aspirin).

no coined names . . . specify . . . **MRT**

literature and samples on request

MARVIN R. THOMPSON, INC.
service to medicine

STAMFORD, CONNECTICUT



for the Treatment of

ARTHRITIS and RHEUMATISM

RAYSAL WITH SUCCINATE . . . The *ethical* salicylate-succinate formula . . . Employs three principal ingredients—salicylate, iodine, and succinate . . . designed to combine the almost specific antiarthritic and antirheumatic action of the salicylates, the stimulating and nutritionally corrective effects of iodine and the salicylate detoxifying action of succinic acid.

An ideal companion medication for other therapeutic measures employed in arthritis and rheumatism. RAYSAL WITH SUCCINATE will enhance the efficiency of RAYFORMOSIL . . . a safe and effective combination for use in your next case. Sample and literature will be sent upon request.

The Detoxified Salicylate Medicament

ENTERIC COATED TABLETS (SALOL)

Raysal.....5 grains
(Representing 43% Salicylic Acid and 3% Iodine in Calcium-Sodium Phosphate Buffer Salt Combination)
Succinic Acid.....2 grains

Available for office use and at your pharmacy on prescription

RAYMER PHARMACAL COMPANY • PHILADELPHIA 34, PA.
PHARMACEUTICAL MANUFACTURERS
Over a Quarter Century Serving Physicians

PENETRATES THE BARRIER OF PATIENT-RESISTANCE IN ACNE TREATMENT

"The intraderm solutions have a singular advantage over other topical applications in that they are simple to apply and there is a notable absence of messiness. There can be little doubt that these features contribute materially to the success of this method. Patients who usually object to the messiness of other preparations are more cooperative with the intraderm regime."[1]

1. Grinnell, E.: Journal-Lancet 68: 121 (1948).

INTRADERM® SULFUR SOLUTION

Skin-Penetrant

Provides the dermatologic benefits of sulfur in a unique skin-penetrating vehicle which carries the medication to the site of the disturbance, diffusing through the affected cutaneous structures.[2]

2. MacKee, G. M.; et al.: J. Invest. Dermat. 6: 43 (1945).

INTRADERM SULFUR is supplied in 30-cc. bottles . . . available through all prescription pharmacies.

Professional Literature on Request

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Modern MEDICINALS

Physicians will find that these brief resumes of essential information relative to the newer medicinals are so prepared that they may be removed and pasted on standard 3x5" file cards, and filed as illustrated in the adjoining picture, for ready reference.

Pyribenzamine

3-49

MANUFACTURER: Ciba Pharmaceutical Products, Inc., Summit, N. J.

INDICATION: Elixir—to combat the pharmacologic effect of histamine or histamine-like substance in the production of allergic symptoms. Valuable in the symptomatic relief of many types of allergy. Hay fever and urticaria are particularly responsive. Asthma, allergic vasomotor rhinitis, atopic dermatitis, physical allergy, gastro-intestinal allergy, and drug reactions are also favorably influenced. Non-specific pruritus is frequently relieved.

Ointment and Cream—topically applied Pyribenzamine exercises a local antihistaminic action thereby alleviating pruritus and allergic skin manifestations. Of value in the treatment of atopic dermatitis, pruritus ani, contact dermatitis, neuro-dermatitis· lichen chronicus simplex. Also for the general alleviation of pruritus in non-specific skin disorders.

ACTIVE CONSTITUENTS: Elixir—Pyribenzamine hydrochloride, 5 mg. per cc., in a pleasantly-flavored vehicle.

Ointment and Cream: Pyribenzamine ointment and cream contain a 2 per cent concentration of the active antihistaminic agent. They are prepared respectively in a petrolatum base and a water-washable vehicle.

DOSAGE: Elixir—Orally. Fifty milligrams three or four times daily constitutes the average adult dosage. Children generally require a slightly higher dosage than might be anticipated on a weight basis.

Ointment and Cream—Topical application. A light dressing should usually be applied following application of the ointment. Significant systemic absorption may occur if ointment or creams are applied to extensive raw areas. In rare instances a contact type of eczematous allergic reaction may occur.

HOW SUPPLIED: In bottles of 16 fl. oz. and 1 gallon. Ointment and Cream—In jars of 50 grams and one pound.

Alzinox

3-49

MANUFACTURER: The E. L. Patch Company, Boston, Massachusetts.

INDICATIONS: In the treatment of hyperacidity and peptic ulcer.

ACTIVE CONSTITUENTS: Plain—Each tablet (white) contains: dihydroxy aluminum aminoacetate 0.5 Gm. (7.7 grains). With phenobarbital and homatropine methyl bromide—Each tablet (pink) contains: dihydroxy aluminum aminoacetate, 0.5 Gm. (7.7 grains); phenobarbital, 16.2 mg. (¼ grain).

DOSAGE: 1 or 2 tablets, 1 to 2 hours after meals and upon retiring.

HOW SUPPLIED: In bottles of 100 and 500.

3 IMPORTANT THERAPEUTIC VALUES IN A SINGLE TABLET

ANTISPASMODIC. Homatropine Methylbromide 1/24 gr. Comparable to 1/50 gr. atropine in antispasmodic effect on the stomach and only 1/54th as toxic.

SEDATIVE. Phenobarbital 1/8 gr. Allays apprehension; relieves nervous and emotional disturbances.

ANTACID-ADSORBENT. Alukalin 5 gr. Kaolin activated with alumina gel.

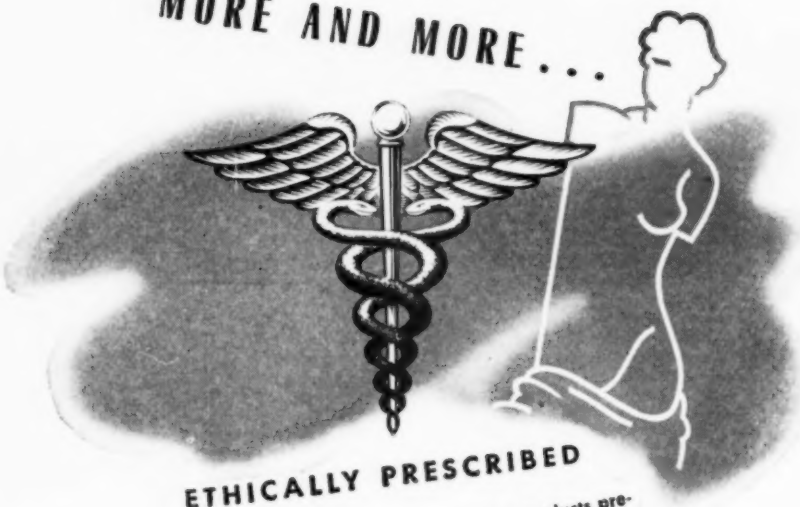
A THREE-FOLD ATTACK ON GASTROINTESTINAL DYSFUNCTIONS

AVAILABLE IN BOTTLES OF 100, 500 AND 1000 TABLETS

NEWARK 1, Matthie NEW JERSEY

FOUNDED 1888

MORE AND MORE...



ETHICALLY PRESCRIBED

Koromex Jelly and Koromex Cream are the companion products prepared by a medically accepted manufacturer incorporating all of these particularly valuable features...A uniformity in pH 4.5, consistent with normal vaginal fluids... spermicidal times less than 3 minutes... bacteriostatic oxyquinoline benzoate... Contain de-ionized water to assure maximum freedom from impurities usually present in ordinary water, thereby eliminating possible unfavorable chemical reaction.

ACTIVE INGREDIENTS: BORIC ACID 2.0%, OXYQUINOLIN BENZOATE 0.02% AND PHENYLMERCURIC ACETATE 0.02%, IN SUITABLE JELLY OR CREAM BASES

FOR MORE COMPREHENSIVE DATA PLEASE SEND FOR AVAILABLE PROFESSIONAL LITERATURE.

KOROMEX

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"CHOICE OF PHYSICIANS"

HOLLAND-RANTOS COMPANY, INC., 145 HUDSON STREET, NEW YORK 13, N.Y.

MERLE L. YOUNGS • PRESIDENT

A new pharmacologic advance for improved therapy!

Tresanoids

antibiotic
rectal
suppositories

they don't melt . . . they dissolve!

TRESANOIDS combine tyrothricin and benzocaine in a soothing, astringent formula with an entirely new, heat-stable (m.p. 48-50°C.), water-washable base.

They Don't Melt . . . They Dissolve!

TRESANOIDS remain firm at room temperature and will not melt even at body heat. Yet TRESANOIDS act promptly because they are water-soluble and disintegrate quickly in the moisture of the rectum, relieving pain and combating gram-positive organisms.

Antibiotic . . . Analgesic

Indicated for antibiotic-analgesic therapy of hemorrhoids, anal fissure, cryptitis, and proctitis, each water-soluble TRESANOIDS suppository releases: *Tyrothricin*, 1 mg.; *Benzocaine*, 15 mg.; *PROPADRINE® HCl*, 20 mg.; *Bismuth subgallate*, 150 mg.; *Zinc oxide*, 150 mg. Supplied in boxes of 12.

For a sample quantity, mail this page and your prescription blank to: Professional Service Dept., Sharp & Dohme, Phila. 1, Pa.

Tersavin

3-49

MANUFACTURER: Hoffmann-La Roche Inc., Roche Park, Nutley 10, N. J.

INDICATIONS: Tersavin combines the bactericidal activity of penicillin with the vasoconstrictor effect of ephedrine. For the treatment of acute and chronic sinus infections.

ACTIVE CONSTITUENTS: Each tablet contains 30 mg. of the crystalline *l*-ephedrine salt of penicillin G (equivalent to 30,000 units of penicillin G and 9.9 mg. of *l*-ephedrine) with suitable buffering agents. When a tablet is dissolved in 7.5 cc. of distilled water, each cc. of the solution will contain approximately 4,000 units of penicillin G and 1/8 per cent of *l*-ephedrine.

DOSAGE: Tablets are dissolved in distilled water and the solution is applied to the infected sinuses by irrigation, instillation or the Proetz displacement technic.

HOW SUPPLIED: In packages of 8 foil-wrapped tablets, together with a bottle graduated at 7.5 cc. in which the solution may be made.

Eskadiamer

3-49

MANUFACTURER: Smith, Kline and French Laboratories Fifth and Arch Streets, Philadelphia 5, Pa.

INDICATIONS: Wherever oral dosage of the sulfonamides is indicated.

ACTIVE CONSTITUENTS: An unusually palatable aqueous suspension of 'Micraform' sulfadiazine and 'Micraform' sulfamerazine. Each 5 cc. (1 teaspoonful) contains microcrystalline sulfadiazine, 0.25 Gm. (3.86 gr.) and microcrystalline sulfamerazine, 0.25 Gm. (3.86 gr.). Thus each teaspoonful contains 0.5 Gm. —the dosage equivalent of the standard sulfonamide tablet.

DOSAGE: One teaspoonful is the dosage equivalent of one standard half-gram (7.7 gr.) sulfonamide tablet. (One fluid ounce equals six half-gram tablets.) As with all sulfonamide drugs, toxic reactions may occur in sensitive individuals. Constant supervision of the patient is essential.

HOW SUPPLIED: In 12 fl. oz. bottles.

Aureomycin Hydrochloride

3-49

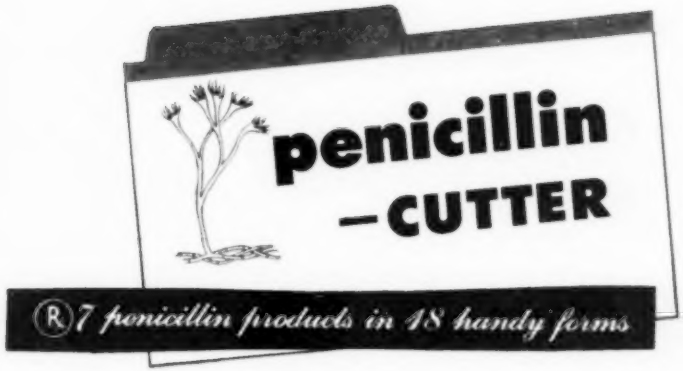
MANUFACTURER: Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.

INDICATIONS: It is highly effective against such rickettsial infections—as Rocky Mountain spotted fever, rickettsialpox, Q fever, and typhus fever. Additionally, certain diseases are now believed to be rickettsial in nature including lymphogranuloma venerem—a venereal disease common in the tropics—psittacosis ("Parrot Fever") and possibly other similar diseases. In certain instances, primary atypical pneumonia, a disease of unknown cause, has appeared to respond dramatically to aureomycin. Certain bacterial infections, previously highly resistant to other forms of chemotherapy have been successfully attacked with aureomycin, including acute brucellosis, resistant staphylococcus infections, and infections caused by those bacteria common in the intestinal tract, the "coli-aerogenes" group. Laboratory and unpublished clinical data indicate that aureomycin given in large dosage may be useful in the control of typhoid fever. In many eye infections including those of a viral-like nature—such as inclusion conjunctivitis, follicular conjunctivities and herpes of the cornea—aureomycin has proven highly effective. Aureomycin may be prescribed for infections that have developed resistance to penicillin, streptomycin, or the sulfonamides; also for patients exhibiting a severe sensitivity to these drugs.

ACTIVE CONSTITUENTS: Aureomycin hydrochloride.

DOSAGE: Toxicity of aureomycin given by mouth is low. Aureomycin may be administered orally in relatively large amounts. Such massive doses as 1 gram, four times a day for several days have been reported. The ophthalmic preparation may be administered by adding 5 cc. of distilled water to 25 mg. of aureomycin.

HOW SUPPLIED: Capsules of 250 mg. in boxes of 16; in powder form with diluent for ophthalmic use.



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Crystalline potassium penicillin G tablets buffered with calcium carbonate. Supplied in vials of 12, 25, 100 in 50,000 unit tablets and 12, 100 in 100,000 unit tablets. May be stored up to 18 months at room temperature.

℞ No. 6—PEN-TROCHES*

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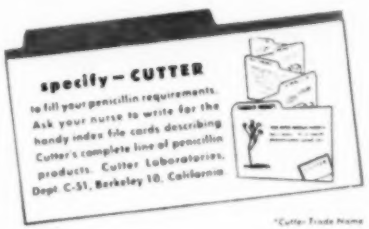

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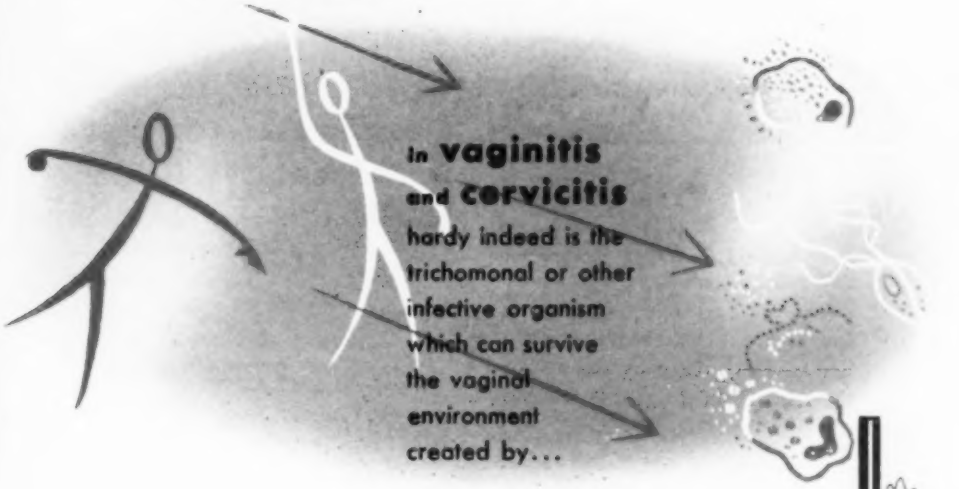

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—Kasdon, S. C., and Cornell, E. L.: Am. J. Obst. & Gynec. 56: 853 (1948).

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"...nutritional deficiency may occur in children and adolescents much more commonly than previously supposed."

—Biskind, M. S., and Williams, R. R.: Am. J. Digest. Dis. 14: 121 (1947).

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—Brougher, J. C.: West. J. Surg. 52: 274 (1944)

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—Touhy, E.: in Handbook of Nutrition. Chicago, American Medical Association, 1943; p. 384.

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1. Caravati, C. M., and Whims, C. B.: General Manifestations of Salicylism, South. M. J. 38:722-726 (Nov.) 1945.
2. Litchfield, H. R.: A Clinical Study of Rheumatic Fever, with Special Reference to Salysal Therapy, Arch. Pediat. 55:135-142 (March) 1938.

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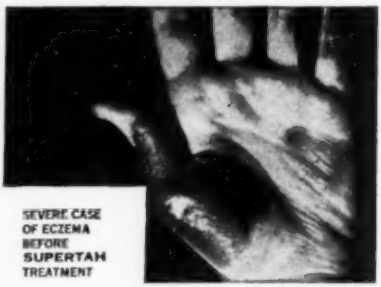

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*Swartz & Reilly, "Diagnosis and Treatment of Skin Diseases," page 66

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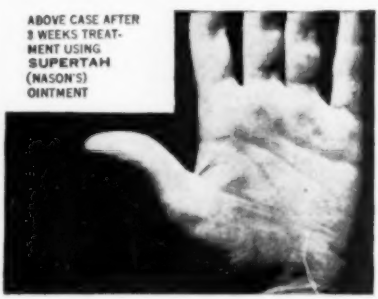

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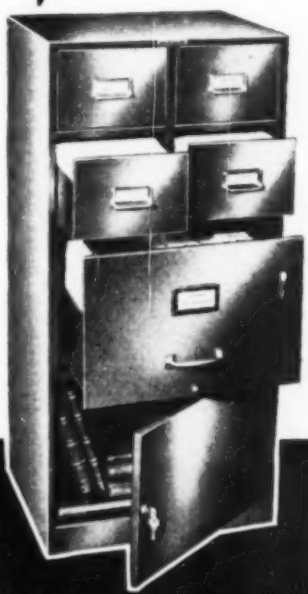

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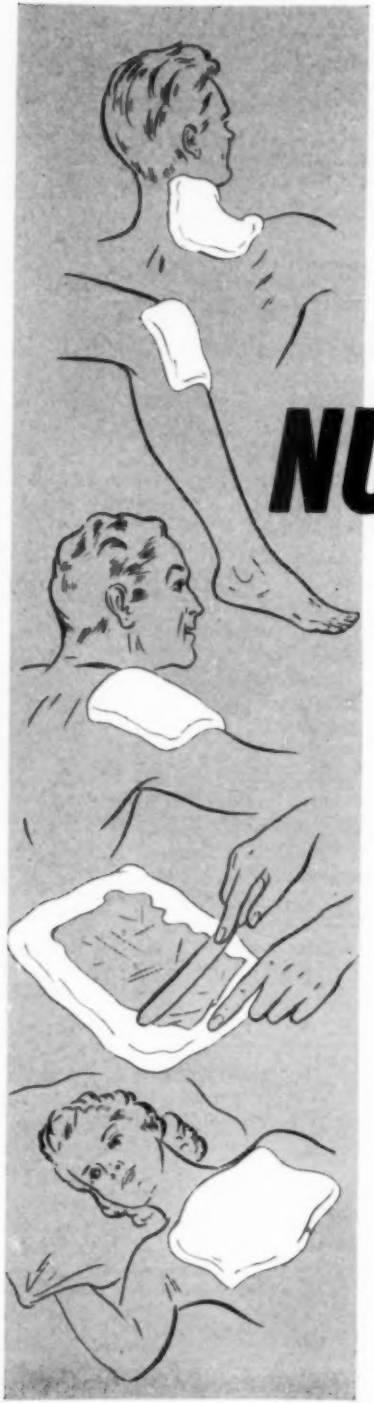

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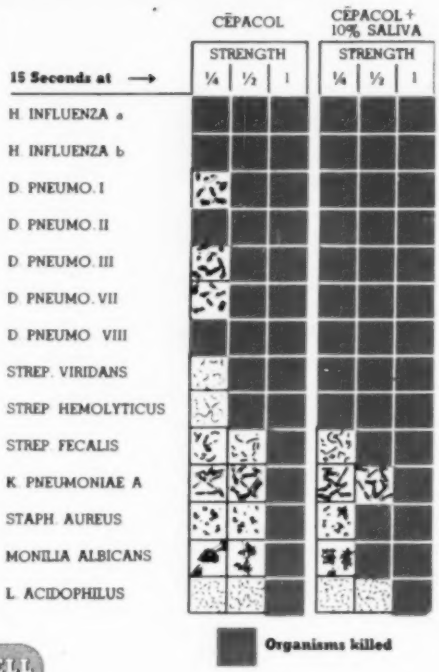

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Pulmonary Embolism

Tadeusz Larkowski, M.D., F.A.C.S.[1] and Albert R. Rosanova, M.D.[2]

Chicago, Illinois

Pulmonary embolism is the immediate cause of death in 2 per cent of all patients even though the patient may have some other pathology present also. The common causes of pulmonary embolism may be divided into surgical and medical. The surgical causes are the most familiar to all of us and the most dreaded. This includes the postoperative, postpartum, and the posttraumatic. This is the cause of 50 per cent of all IMPORTANT postoperative complications. The medical causes most commonly encountered are bacterial endocarditis, auricular fibrillation and phlebitis.

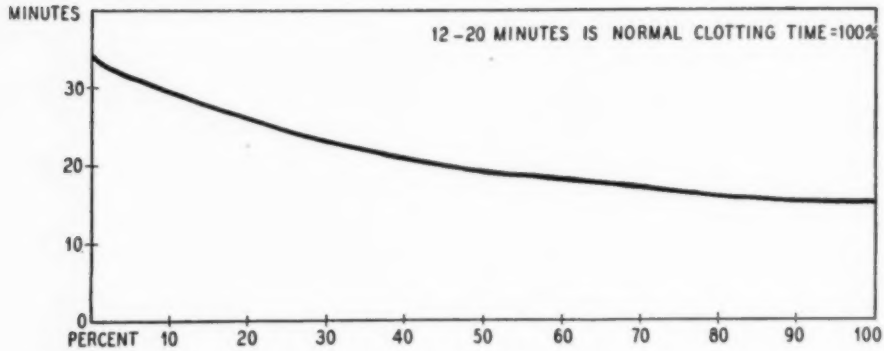
There are many THEORIES as to why the blood clots, with their subsequent emboli, form. Amongst these are the breaking off of emboli from vegetations in the heart in subacute bacterial endocarditis, and in auricular fibrillation. Prolonged bed rest with consequent circulatory retardation is worse in its effects in the presence of cardiac failure. Dehydration increases the blood viscosity. Malnutrition associated with hypoproteinemia and an increase in the plasma fibrinogen and calcium favors thrombus formation. Clumps of neoplastic tissue or infected tissue make a nidus around which a clot can form. Finally, there is the blood sludge theory which states that in disease the blood cells clump together easier and thus tend to form clots easier. These are some of the theories that have been advanced to explain the phenomenon as to why the blood clots easier in certain instances than in others.

The pathology involved in pulmonary embolism is usually the occlusion of one of the main pulmonary arteries. Occlusion of this main blood vessel causes widespread pulmonary edema without hemorrhagic consolidation. However, atelectasis may occur due to constriction of a bronchus. This may be promptly fatal. Occlusions of the smaller lung vessels cause only infarcts. These vary in size from that of a pea to an orange. They are mostly found in the lower lobes, usually involving the pleura. Grossly on examining a lung with a recent infarct the area is dark. Older infarcts are red brown in color. They are hard and firm. On section they look like an ordinary clot. Microscopically the alveoli are distended with red blood cells.

The main symptoms if a large pulmonary artery is involved consist of a sudden onset with pain in the chest which is severe and substernal. The patient becomes anxious and complains of a tightness in the chest. Cyanosis and dyspnea are present. Pulmonary edema occurs. Fever ranges from 99 to 104 degrees Fahrenheit orally. Shock is present with a fast, feeble, thready pulse. The blood pressure is low. Death may follow within a few minutes to several hours. If a smaller pulmonary vessel is involved the onset is also sudden with pain in the chest which is pleuritic in nature. Cyanosis and dyspnea appear. Shock symptoms may or may not occur depending on the extent of the involvement. Fever may or may not occur also depending on extent of involvement. Physical examination shows signs of consolidation if the infarct is large enough. X-rays are not diagnostic early. Later they may show the triangular shaped infarct area.

In the Differential Diagnosis of pulmonary embolism one must consider the differences between infarct and embolism as given above and also pleurisy, pneumonia, atelectasis, coronary occlusion and angina pectoris. Pulmonary embolism may

1. Attending Staff St. Mary of Nazareth Hospital, Chicago, Ill. Clinical Professor, Loyola University Medical School.
2. Attending Staff St. Mary of Nazareth Hospital, Chicago, Ill. Clinical Instructor, University of Illinois Medical School.



occur in combination with any of these diseases. A differential diagnosis in this type of case may be impossible.

Prevention is the most important thing in the treatment of pulmonary embolism. In the surgical cases early ambulation with deep breathing exercises and frequent moving about of the patient postoperatively is important. Prophylactic ligations of the superficial femoral vein, in pelvic surgery cases in which extensive procedures have been done, is practiced by many men. Heparin and dicoumarol may also be given prophylactically. The exact dosages will be presently discussed. One must always be on the lookout for phlebothrombosis after surgery. This is recognized by pain in the legs with tenderness in the calves. Homan's sign, which is a painful discomfort in the calf on dorsiflexion of the foot, is positive. If there are any pulmonary symptoms at all postoperatively, always check the legs for signs of phlebothrombosis.

Prophylatic treatment in the medical cases consists of moving the patient about frequently. Prevent pressure of leg against the mattress. Watch the nutrition and hydration. Dicoumarol and heparin may be given prophylactically.

In the active treatment of pulmonary embolism one must first treat the shock. Oxygen is given at once. Morphine is given to relieve pain and anxiety, even in the face of cyanosis and collapse. Papaverine hydrochloride 1½ grains with atropine sulfate 1/150 grain is given intravenously to block off vagal effects and relieve spasm of the surrounding bronchi and vessels. However, some men claim that papaverine is of no value and may be harmful. It has been found to be of value in our hands.

The anticoagulants heparin and dicoumarol are used as follows. Heparin is best given in watery solution. There are various oily preparations and the so-called Heparin Pitkin Menstruum, which are all very good for maintaining the increase in blood coagulation time for a 24 to 48 hour period. However, the authors prefer the watery solution. The heparin comes in 10 cc. vials. Each cc. is equal to 1,000 units. No more than 20,000 units or 20 cc. are given over a 24 hour period. The blood coagulation time must be maintained between 15-20 minutes. The heparin is best given in 1,000 cc. of 5 per cent glucose intravenously, giving only 25 drops per minute. Or it may be given in 5 cc. doses, four times a day.

Dicoumarol takes 12 to 24 hours to start its action; therefore, heparin is given the first 24 hours with the dicoumarol, and after 24 hours the heparin is stopped and the dicoumarol alone is given. The dicoumarol is given in 100 mg. doses three times a day for 2 to 3 days. The dose is immediately decreased when the percentage of the PROTHROMBIN TIME is reduced to 50 per cent of normal. The prothrombin time is determined by adding .1 cc. of thromboplastin reagent (Difco Laboratory) to 1 cc. of plasma. The normal blood clots

in 12 to 20 minutes. This is considered as 100 per cent. The following graph may be helpful.

The toxic effects of heparin and dicoumarol are a very important consideration. Dicoumarol has an accumulative effect; therefore, it is best stopped in 12-14 days. Some men continue dicoumarol in 50 mg. dosages per day for months at a time with no bad results (especially in coronary thrombosis cases). Heparin and dicoumarol if used carelessly may cause hemorrhages in the body, especially in the brain, and thus cause death.

The treatment of hemorrhage due to heparin and dicoumarol therapy is to give 100 mgm. of vitamin K daily intramuscularly until coagulation time is restored to normal. Protamine sulfate may be given in 1 cc. dosages. This is a fish protein, and has been used successfully by Dr. Iason (personal communication). Blood transfusions, calcium, coagulen, thromboplastin, ceanothyn, and others may all be tried in stopping the internal capillary hemorrhage due to anticoagulant therapy.

Contraindications to the use of heparin and dicoumarol are liver damage, and blood dyscrasias of any type. Never give either one if the blood coagulation and prothrombin time cannot be adequately watched. Never start heparin or dicoumarol therapy earlier than 4 hours after any surgery because the patient may bleed to death.

In the surgical treatment of pulmonary embolism, embolectomy and ligation of vessels are done. Embolectomy of the large pulmonary vessels of course is a shock-producing procedure in itself. The patient already is in shock from the embolism so that the mortality is high. Even after a successful operation, new thrombi and emboli form and cause subsequent death of the patient. Embolism of smaller pulmonary vessels of course is treated medically as stated above. Embolism in the extremities is not the subject of this paper but in passing we may say that ligation of the affected vessels proximal to the site of the embolism (if the embolus is in a vein) combined with paravertebral blocks and anticoagulant therapy, or embolectomy if the embolus is in an artery, is the treatment of choice.

Summary

Emphasis has been placed on the detailed prophylactic treatment in both medical and surgical cases so that the incidence of embolism may be lessened. An understanding of the etiological factors involved is helpful in this respect. In the final analysis, prevention is the best treatment. Detailed discussion of the newer anticoagulants and how to use them is also given.

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American Geriatrics Society

The sixth annual meeting of the American Geriatrics Society will be held June 2, 3, 4, 1949, at the Hotel Brighton, Atlantic City, New Jersey.

SPECIAL ARTICLE

Amebiasis

This summarization attempts to cover all of the known therapeutic information on the subject and is designed as a time-saving refresher for the busy practitioner.

Reprints available*

Amebiasis, also known as entamebiasis, is the condition in which human tissues are invaded by the *Endamoeba histolytica*, a protozoan parasite. Included under this general term are amebic colitis and amebic dysentery.

Incidence

Amebic dysentery or tropical dysentery is sometimes considered to be a tropical disease but this is not true because the first case was described in St. Petersburg, Russia, in 1875.[1] In 1890 the first case was reported in the United States[2] and in 1891 the pathology of this disease was described. It was not until 1913 that *Endamoeba histolytica* was established as the etiologic agent. The disease was produced by feeding the parasite to humans.[3] Although amebic dysentery is the better known form, there are many cases of the milder, more chronic form of amebic colitis.[4] It was not until the outbreak of amebic dysentery in Chicago 15 years ago that the presence of this disease in the United States was considered of importance. Since that time the number of cases has increased considerably and *Endamoeba histolytica* has been found in about 10 per cent of the patients examined.[5]

Some feel that this is a conservative estimate and that 20 per cent is more accurate.[6] Another survey of a Chicago hospital for 12 years including the epidemic years revealed an incidence of 7.9 per cent among 2000 patients and employees.[7] A study of the food-handling inmates of a New York hospital for the insane showed that 13.9 per cent were carriers.[8] Two investigations of returning military personnel showed 8.9 per cent of 1000 who returned from the Pacific were infected and 16.8 per cent of 1000 from the European area were infected.[9, 10]

A study of statistics shows that a median figure of 961 was calculated as the number of cases occurring in any 6 months' period between 1943-1947 but the total number of cases for the first six months of 1948 was 1,988 or more than double. This figure is probably lower than the actual number of cases. Although the number of cases has been increased considerably since the war, at present authorities do not believe that it is due to returning service men but they are holding this theory in reserve as a possibility.[10a]

In the United States amebiasis is more commonly found in the west south central states of Louisiana, Arkansas, Oklahoma and Texas. The New England states have the lowest incidence whereas the southern states in general have a higher incidence than any other section except possibly the Pacific coast states.

The poorer races generally show a greater incidence of amebiasis because of poor sanitation. It also is more predominant in the warmer areas because the cyst

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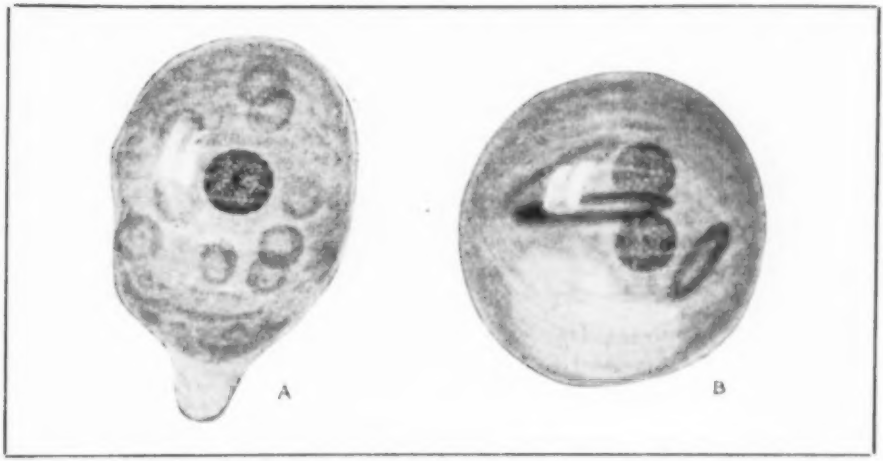

Fig. 1. **Endamoeba histolytica** ***stained with iron hematoxylin. A. Trophozoite, B. Cyst.***

has a more favorable environment in which to exist outside of the human host.

Etiology

There are 5 species of *Endamoeba* which may be found in the intestinal tract of man as follows: *Endamoeba histolytica, Endamoeba coli, Endolimax nana, Iodamoeba butschlii* and *Dientamoeba fragilis.* Amebiasis is caused by *Endamoeba histolytica.* The other organisms are relatively harmless. There are two groups of *E. histolytica,* known as the large and small races. The former race is pathogenic in experimental animals and humans but the latter is much less virulent and may even be harmless. *Endamoeba histolytica* is named thus because of its ability to dissolve man's tissues. It was first described by Schaudinn in 1903. This organism causes lesions generally in the large intestine resulting in varying degrees of amebic colitis. In more severe cases amebic dysentery is observed to be present as shown by the passage with pain of bloody, mucoid stools. As the condition progresses secondary lesions may develop in the liver. The organism can be isolated from the lesions either in life or after death of the patient. The disease can also be brought about experimentally in humans and animals. Attempts at culturing the organism have failed unless there are bacteria present.[11]

Life Cycle

Endamoeba histolytica exists in two stages: the active or vegetative stage known as the trophozoite and the inactive or resistant stage known as the cyst. There also may be an intermediate or precystic stage. In the active or vegetative stage the trophozoite moves about, feeds and reproduces. The motility is accomplished by means of pseudopodia and is generally characteristic of the species. Examination of the cell reveals only one nucleus unless the trophozoite is dividing or if the organism is *D. fragilis* rather than *E. histolytica* or one of the others previously mentioned. Food vacuoles are contained in the endoplasm and serve as reservoirs for all ingested bacteria, red cells and food particles. Binary fission is the process by which the trophozoite reproduces. At certain times and in certain environments the trophozoite rounds up, extrudes all undigested food matter, decreases in size, and is no longer motile. This is called the precystic stage and is followed by the secretion of a cyst wall and food is stored in glycogen vacuoles or as chromatoid matter in bars, splinters or granules. This is the cyst stage. The

food material enveloped is gradually absorbed and nuclear division into as many as eight nuclei may result in the maturation process. *D. fragilis* is believed to be the only one of the species which does not form a cyst.[5]

Because the nuclei and the cyst of *E. histolytica* are spherical, the chromatoid matter is in round bars and the glycogen vacuole is globular it may be difficult to observe under the microscope. Changing the focus may be necessary to see the entire structure. In wet preparations the cysts may roll across the field. The *Endamoebae* are differentiated from the other genera by the structure of the nuclei. The karyosome is relatively small and the inner surface of the nuclear membrane has a layer of chromatin granules so that in optical section the nucleus resembles a cart wheel. Very careful staining is necessary to differentiate the species of *Endamoeba* and the points which are important are the size and position of the karyosome and the deposition of chromatin granules on the nuclear membrane.[5]

The trophozoite form of *E. histolytica* is very sensitive, is affected by slight changes of temperature, and normal digestive juices destroy it. In order to maintain the trophozoite alive it is necessary to keep it moist and in an environment in which the osmotic pressure is the same as that of tissue fluids. Its rate of infectivity is not very high. The cyst stage is much more resistant and can survive room temperatures for 2 to 4 weeks. Freezing, chlorine in the standard concentrations employed for purifying water, and normal digestive juices of the stomach and intestine do not affect it. Quick drying, boiling or exposure to 55° C. temperature for a few minutes will destroy the cyst, the infective form. [5, 11]

Transmission

Although parasitic organisms considered to be *E. histolytica* or closely related to it have been isolated from monkeys, rats, dogs and pigs which were naturally infected, man is considered to be the principal reservoir host. Although flies, and in particular the filth flies, are capable of being mechanical vectors, no intermediate host is necessary. Thus the parasite is transmitted directly from man to man.

The host for *E. histolytica* may have only mild symptoms of amebiasis or none at all for the parasite may live in the lumen of the bowel without causing any trouble for the host. The trophozoite stage thus obtains its nourishment from the fecal stream and accordingly multiplies. If bowel activity is normal the trophozoite can pass into the cyst stage before it is eliminated in the formed stools. If the trophozoite invades the bowel wall, resulting in ulceration and dysentery, and is carried by the blood stream to other parts of the body, the fecal elimination will be liquid and generally contain trophozoites rather than cysts. In such cases the stools will be bloody due to ingestion of red cells by *E. histolytica*. Thus the host who eliminates formed stools is the more dangerous individual because he is eliminating the greater infective agent. Experimental animals have been found to develop the infection after being fed trophozoites but in actual living conditions the trophozoite rarely survives the action of the gastric secretions and rarely reaches a new host.[5, 11] There are many ways by which humans acquire or transmit this infection. They are as follows: (a) direct contact with the unwashed hands of a carrier ("cyst-passer") or a convalescent; (b) ingestion of food or drink contaminated by carriers serving as food handlers; (c) swimming in polluted pools; (d) ingestion of uncooked vegetables or fruits which have been washed with polluted water or grown in soil fertilized with human excreta; (e) drinking of contaminated water; and (f) transmission by flies carrying the cysts on their legs or in their excreta.[5, 11] Studies have shown that cysts are still viable in excreta of flies 48 hours after they have fed on infective material.

Invasion of the Tissues

After the cyst has been ingested by one or another means of transmission it passes without interference through the stomach and small intestine and, finally, in all probability to the lower ileum where excystation occurs. A pore in the cyst wall

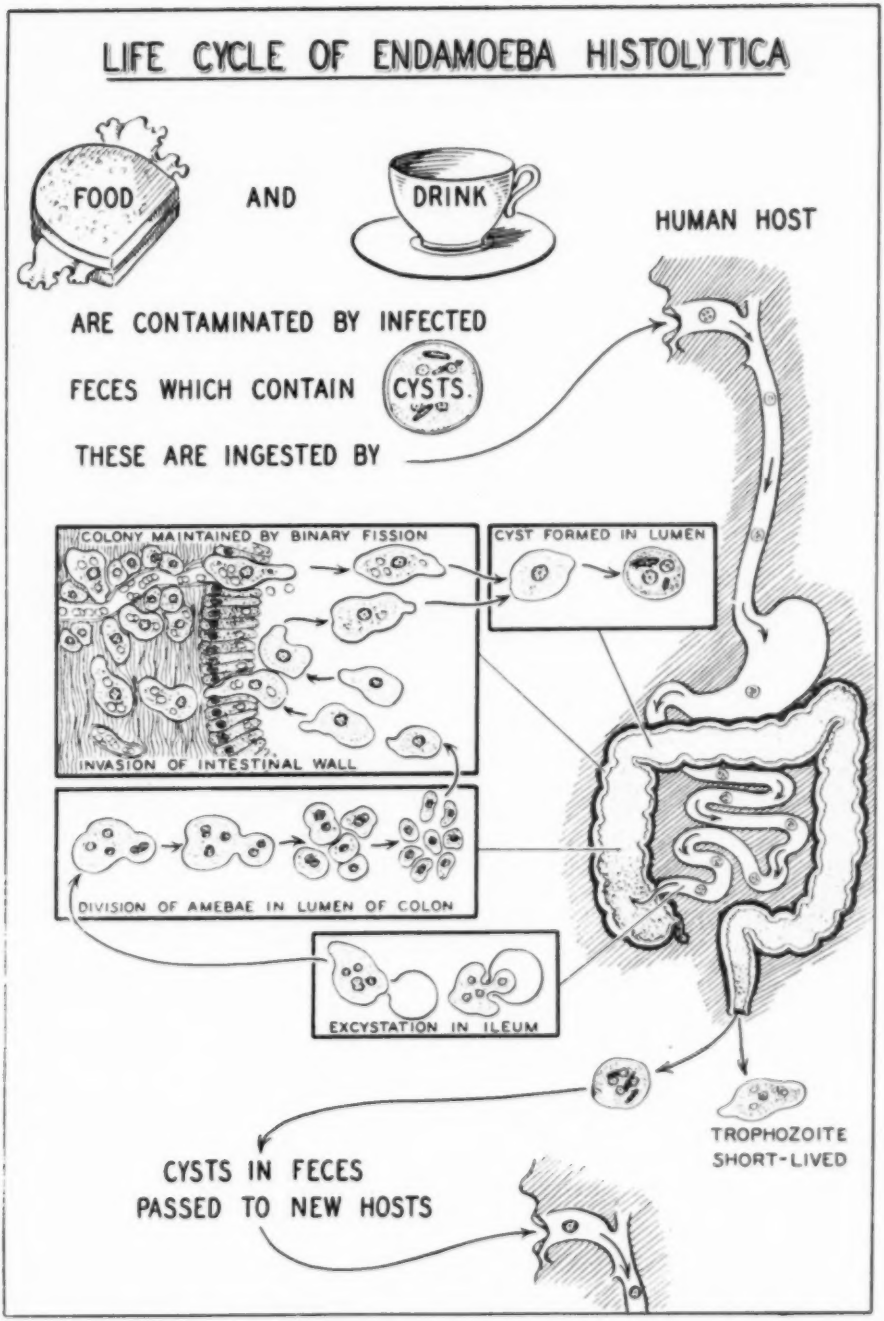

Fig. 2. Location and degree of colonic lesions indicated by depth of shading.

opens to allow the ameba to escape and it passes into the colon where it grows and by fission develops into a colony of trophozoites.[5, 11]

Following the ingestion of the cyst the infection may develop into the clinical disease or into an asymptomatic carrier condition. The incubation period of the infection varies considerably from one to several weeks.[5] One authority has observed incubation periods of 20, 57, 87 and 95 days.[12]

As the trophozoites develop they begin the penetration of the mucous membrane of the cecum, appendix, ascending colon, sigmoid colon and rectum by direct phagocytosis and by the liberation of cytolysins. The lesion formed is chiefly necrotic and may not show inflammation unless accompanied by a secondary bacterial invasion. A flask-shaped or buttonhole ulcer is formed by the narrow burrowing of the ameba into the mucosa and the extension of the area in the submucosa. The extent to which these ulcers spread is dependent upon the resistance of the patient and the promptness with which therapy is instituted. As the disease progresses the focal and discrete lesions spread until they become confluent. Edema, hemorrhage and sloughing off of large areas of mucosa may accompany the enlargement of the lesions. The ameba may be stopped by the muscular coat in most cases, in others this may also be penetrated and perforation occurs. Further progression of the disease results in the entry of the amebae into the portal vein through the radicles from whence they pass on to the liver. Hepatitis also known as miliary necrosis or abscesses may result if the parasites are sufficiently numerous to survive. Examination of these abscesses shows that the amebae are generally found in the margin of the hepatic tissue which remains. The abscesses are usually single in nature and located in the right lobe of the liver. Intestinal bacteria may be present and cause a secondary infection. If the disease is allowed to progress further, the pleura is next affected, then the right lung and the pericardium. An alternate route which it may follow is along the tracts which a liver abscess follows in surgical drainage. Lesions in almost every organ of the body have been observed in rare cases. Ulcers of the skin may be observed following surgical drainage of the abscess or they may extend from the rectum to the anal and penile regions.[13] Amebiasis also has been reported as responsible for urticaria, angioneurotic edema, exfoliative dermatitis and granulomas of the bowel.[14, 15] Urinary amebiasis is considered to be rare.[16]

Symptoms

Most patients infected with *E. histolytica* do not develop a serious illness or definite pathologic condition but a small percentage do. Individuals who are in an asymptomatic state or a carrier state may later develop definite clinical symptoms or they may pass it on to others who in turn develop a clinical illness. Patients who have a mild case or have been cured supposedly may suddenly show the symptoms of dysentery or hepatitis. It is believed that many symptoms do not appear until the ulcerations are of considerable size.[11]

A. Amebic Colitis

Amebic colitis is usually considered to be the mild manifestation of the infection. The following symptoms are generally observed although they do vary and particularly are influenced by the type of infection: constipation; mild, lower abdominal cramps; nausea; anorexia; gaseous distention; belching; dull aches in the head, back and extremities; flushing of the skin; tachycardia; sweating but little or no fever; and mild and evanescent diarrhea, if present at all. The diarrhea may occur only when preceded by excesses in consumption of food and alcoholic beverages. There may be a feeling of depression, somnolence and fatigability on the part of the patient. The clinical picture is usually that of an "irritable colon" and deep pressure over this organ, especially in the cecal region, may reveal moderate tenderness. Gross examination of the stools generally shows them to be normal except during the periods of diarrhea.[5, 11]

B. Amebic Dysentery

Amebic dysentery may be acute or chronic in nature. The acute type is usually sudden in onset and is accompanied by a headache, cramps, nausea, vomiting and a diarrhea which increases in severity (5 to 20 liquid stools daily). Tenesmus if present is mild. The stools are usually brown in color but gross examination will reveal patches of mucus and blood. Microscopic examination of these would probably reveal enormous numbers of amebae. There may be localized abdominal tenderness; little or no fever; and an increased leukocyte count as high as 20,000 per cm. The condition has a gradual development and remission and has a tendency to assume a chronic course (walking dysentery) in which there are alternating periods of amebic colitis with constipation and amebic dysentery with diarrhea. In the remission periods in which there is amebic colitis there is usually a severe weight loss and an increasing moderate anemia. The relapses of the dysentery phase may occur fairly frequently or they may not occur for 20 or more years.[11]

The chronic amebic dysentery may also develop as a result of inadequate therapy of the acute attack.[17]

C. Amebic Hepatitis and Liver Abscess

Amebic hepatitis and liver abscess are complications which accompany amebic dysentery. Either may be present without the other. They generally result after repeated attacks of the dysentery but may develop without any previous intestinal symptoms (10 to 40 per cent). Although these complications are more frequently found in individuals living in tropical areas where sanitation is poor, many cases have been reported in the temperate zone. Hepatitis may precede the development of the abscess by 4 or more weeks. Differentiation is made by the fact that a course of emetine therapy for 2 to 3 days will result in elimination of the symptoms in hepatitis. The onset of amebic abscess may be gradual or sudden. It is accompanied by pain which may be dull and aching or severe and sharp located generally in the right upper quadrant and frequently in the epigastrium, in the right axilla or under the right scapula. The nature of the fever often suggests a bacteremia or malaria because it is very irregular and frequently of a high degree. A total white cell count shows an elevation to 20,000 to 60,000 per cm. and further examination reveals that they are chiefly polymorphonuclear. Physical examination will show an enlarged and frequently tender liver and percussion with the fist over the front of the right lower ribs or finger pressure in the interspaces will show tenderness. Jaundice is generally not present. As the lesion progresses it may cause the right diaphragm to become elevated and fixed and effusion of the right pleura as revealed by roentgenological examination and clinical signs. If the patient develops a severe cough accompanied by a blood or chocolate colored sputum containing trophozoites the lesion probably has broken through the wall of the right lung.[11]

Diagnosis

In the diagnosis of amebiasis it is necessary to differentiate it from various other conditions having symptoms closely resembling those of amebiasis. The symptoms for mucous colitis and mild amebic colitis are practically identical so that it is almost impossible to differentiate the two. Despite the fact that *E. histolytica* may be found in the stools and therapy for amebiasis causes improvement there is still a possibility that the colitis may not be caused by amebae. Tuberculosis and brucellosis must be eliminated as possible conditions if the symptoms of colitis include chronic fatigue and feverishness accompanied by few if any intestinal symptoms.[11] Chronic amebic dysentery closely resembles idiopathic ulcerative colitis in the clinical aspects.[17]

In some few cases of amebic dysentery the attack may be fulminating although this is more common in bacillary dysentery or in cases caused by both ameba and bacillus. However, if the attack is fulminating it closely resembles acute appendicitis so that a careful diagnosis must be made. Amebiasis also should be considered as a possibility in cases of chronic appendi-

citis.[13] It has been reported that during a clinical or subclinical infection due to amebae there may be observed symptoms of subacute appendicitis which may be brought on by the fact that the appendix and cecum have been invaded by the amebae. It is important, therefore, in such cases to delay surgery for 48 to 72 hours and administer emetine and ascertain whether it has any effect. Immediate surgery is almost certain to result in peritonitis and possible death.[11] In diagnosis it is necessary to differentiate between amebic dysentery and bacillary dysentery, colon malignancy, chronic surgical conditions, balantidial dysentery, schistosomiasis, regional enteritis and tuberculous enterocolitis. Amebic dysentery is rarely an epidemic disease as is bacillary dysentery and seldom is found in infants. The course of bacillary dysentery is more frequently fulminating and results in sudden prostration and shock. A patient with amebic dysentery as a rule has a lower fever and a higher leukocytosis. Examination of the stool will show a scanty, watery type of stool with very little fecal matter but containing masses of white mucus flecked with bright red blood in bacillary dysentery whereas in amebic dysentery the stool is fluid, fairly copious, chiefly fecal in character, a dark-brown or reddish color due to varying amounts of fresh or altered blood, blood-streaked or brownish mucus and usually a fetid odor. In amebic dysentery there will be observed microscopically the amebae, a few pus cells and phagocytic cells, a few clumps of erythrocytes scattered throughout, and mucus. The white cells observed in the stools of amebic dysentery patients usually show cytolysis and have a scanty ragged cytoplasm with pyknotic nuclei. The presence of Charcot-Leyden crystals suggests amebic dysentery but they may also be found in other bowel hemorrhage conditions. Proctoscopic examination in a simple case of amebic dysentery generally is negative or may reveal a few scattered ulcerations with normal mucosa in between. Bacillary dysentery is usually accompanied by a diffuse catarrhal colitis which generally does not occur in amebic dysentery.[11]

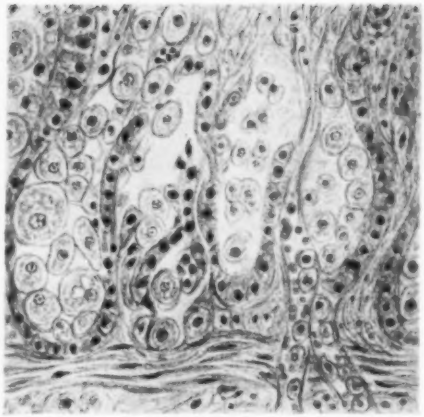

Fig. 3. Section of colon showing* Endamoeba histolytica *in the gland crypts and invasion of submucous and muscular coats by means of a small vessel.

The symptoms of amebic hepatitis or abscess closely resemble those of acute cholecystitis or cholangitis, malaria, appendicitis, subphrenic abscess, pulmonary tuberculosis, pleurisy with effusion and atrophic cirrhosis of the liver as described by Laennec. In this type of amebiasis the patient usually has a tender feeling over the liver and fluoroscopic examination usually reveals a fixation or deformity of the right hemidiaphragm. In order to firmly establish diagnosis the liver fluid must be aspirated. Although generally amebae cannot be isolated from this fluid the physical appearance of the fluid (like chocolate or anchovy sauce) is usually sufficient.[11]

Positive diagnosis of amebiasis is made generally after the presence of *E. histolytica* has been demonstrated in the feces, in tissues or in material from other sources. It is necessary to differentiate the pathogenic from the nonpathogenic forms of amebae. The trophozoite form is identified by the various characteristics described previously. It is generally found in liquid or mushy stools and rarely in the formed stools; in flecks of blood and mucus adhering to the formed stools; in mucus aspirated or draining from an amebic abscess; from the base of specific ulcers; in mucus aspirated from

the lumen of the rectum or from rectal ulcers during proctoscopic examination; or in sputum if the lungs are involved.[5, 11]

In order to obtain the stools for examination it may be necessary to administer a saline cathartic or physiologic saline enema.

The material which is to be examined should be maintained as closely as possible at body temperature until the time of examination which should not be more than 10 or 15 minutes after removal. A warm stage should be used. This enhances the motility. Some workers recommend that the material be centrifuged, followed by zinc sulfate flotation so as to provide a better specimen.[18] Castor oil, liquid petrolatum, barium or bismuth should not be present as they lead to interference in recognition.[5, 11]

Cysts usually will not be found in the aforementioned materials but will be found in formed stools. The cystic form may be recognized by the characteristics described previously.

If the formed stool cannot be examined immediately it may be preserved in a tight container under refrigeration for 48 hours or more. Some workers recommend that two smears be made from each stool, one from the surface and one from the inside. They also have found that an experienced technician can recognize the organisms in 75 per cent of cases in a single specimen and practically all in a series of 3 stools, one of which may be mushy.[5] Others have found that with all the methods used only 30 to 50 per cent of cases can be diagnosed following examination of one stool and at least 3 to 6 stools must be negative before a negative diagnosis can be made definitely in 80 to 90 per cent of cases.[11]

A preliminary examination of feces may be made in an unstained wet smear, using as diluent physiologic saline solution, saline-iron-hematoxylin solution or tap water. The living trophozoites and cysts are usually observed. The saline-iron-hematoxylin solution (add 15 ml. of 0.5 per cent hematoxylin stain solution and 0.25 ml. of 4 per cent ferric amonium sulfate to 75 ml. physiologic saline) has some advantages over the others in that it clumps or coagulates fecal debris and stains the background. The parasites are free in a clear field and their refractility is increased. Blue filters are also of value. Less time is required to locate the trophozoites and cysts and the procedure is less wearing on the eyes. In order to differentiate rounded-up trophozoites from cysts tap water is the medium to use because it provides osmosis due to its hypotonicity which does not affect cysts.[5]

Wet smears may be stained with iodine using Lugol's or D'Antoni's iodine solution to better observe the cysts. The smear is made with tap water to eliminate bastocysts and trophozoites and a toothpick or applicator, dipped in the solution until it is slightly tinted, is used to stir the smear. If cysts are hard to find, when one is located it may be stained by introducing the iodine solution under the coverglass by capillary attraction. Lugol's solution is prepared as follows: Iodine crystals, 5.0 Gm., potassium iodide, 10.0 Gm. and distilled water to make 100.0 ml. D'Antoni's iodine solution is made up of a 1 per cent solution of potassium iodide (prepared from a 10 per cent potassium iodide solution prepared by the specific gravity method) to which is added 1.5 Gm. of iodine crystals for each 100 ml.

Stained fixed smears also may be prepared by the short or long method. The long method is as follows:

1. Fix in Schaudinn's sol. and acetic acid	60 min.
2. Dehydrate in alcohol, 50 per cent followed by 70 per cent, each	5 min.
3. Alcohol, 70 per cent, with iodine to port-wine color	10 min.
4. Alcohol, 70 per cent, to remove iodine	10 min.
5. Alcohol, 95 per cent	5 min.
6. Hydrate in alcohols, 70, 50 and 30 per cent, each	5 min.
7. Distilled water	5 min.
8. Mordant in 4 per cent ferric ammonium sulfate	6 to 12 hr.
9. Rinse in three changes of distilled water.	
10. Stain with 0.5 per cent hematoxylin	12 to 24 hr.
11. Rinse in distilled water.	
12. Decolorize in 1 per cent ferric ammonium sulfate	5 to 8 min.

The slides should be removed from time to time and placed in water to check the

decolorization process. Cover the wet film with a coverglass and examine under the microscope to see if the solid black objects are becoming clearer. Continue decolorization with examination at 1 minute intervals until the desired intensity is obtained.[3]

13. Wash in running water	20 min.
14. Dehydrate in graded alcohols, 50, 75, 95 per cent, and absolute, each	5 min.
15. Clear in two changes of xylene	each 5 min.
16. Mount in balsam.	

The short staining method is as follows:

1. Fix in Schaudinn's solution at 60° C.	2 min.
2. Alcohol, 70 per cent; alcohol, 70 per cent with iodine; alcohols 70 and 50 per cent, each	2 min.
3. Wash in running water	2 min.
4. Two per cent iron-alum at 40° C.	2 min.
5. Wash in running water	3 min.
6. Aqueous hematoxylin, 0.5 per cent	2 min.
7. Wash in running water	2 min.
8. Differentiate in cold aqueous iron-alum solution	
9. Wash in running water	10-15 min.
10. Immerse in 70, 80, 90 per cent, and absolute alcohol, each	2 min.
11. Clear with xylol	
12. Mount in xylol-balsam or clarite.	

Distortion of the organisms will result if the smears are allowed to dry before staining.

There are varying opinions as to the efficacy of stool examination in the diagnosis. One authority recommends the following procedure: (a) Examine 2 formed stools for cysts by using the zinc sulfate method and iodine stains; (b) If negative, give the patient magnesium sulfate or sodium sulfate on an empty stomach and examine the resulting stool for trophozoites; (c) If still negative, give the patient an enema of physiological saline solution at body temperature, examine sediment of enema for trophozoites, introduce proctoscope and examine on a warm stage any mucus or contents of ulcers which may be obtained.[11]

The zinc sulfate method is a concentration method which is helpful when the organisms are scarce but it is time-consuming. It is carried out as follows:[15]

1. Mix one part of formed cyst-bearing stool with 10 parts of warm water in a glass container.

2. Strain 10 ml. of the mixture through 1 layer of wet cheesecloth placed in a glass funnel into a test tube.

3. Centrifuge filtrate for 45 to 60 seconds at 2500 revolutions per minute.

4. Pour off supernatant liquid, suspend sediment in distilled water and repeat centrifugation. Repeat, if necessary, until supernatant liquid is clear.

5. Add to the final sediment 3 to 4 ml. of zinc sulfate solution (33 per cent, sp. gr. 1.180), mix and fill tube with zinc sulfate solution to within ½ in. of the rim.

6. Centrifuge for 90 seconds.

7. Using a loop transfer material from surface of liquid to a slide, stir in 1 drop of dilute iodine solution, cover with a coverglass and examine for cysts.

Another authority states that the following routines are usually successful: (a) Examine the formed stool for cysts for 6 consecutive days if necessary but in 65 per cent of the cases diagnosis can be made the first day; (b) If time is short the patient should be given a magnesium sulfate purge and the formed stool and the first 3 fluid stools following should be examined for trophozoites. Usually they will be found in the third fluid stool. Ninety-five per cent of all cases can be diagnosed with this routine in the first day but some may require a second day.[12]

In the hands of skilled technicians, *E. histolytica* can be cultured on Locke egg-serum medium but this is only of value in detecting the large race organisms. The medium is prepared as follows: Wash 6 eggs with alcohol, break them and emulsify with 75 ml. of sterile Locke's solution. Place 4 ml. in each of a number of test tubes, slant in an inspissator and heat at 70° C. until the medium is solid. Then autoclave at 15 lbs. pressure for 20 minutes. Cover each slant with 4 ml. sterile Locke's solution and serum (10-1) and add a small quantity of sterile rice starch. Check the sterility and then store ready for use.[5]

Complement fixation tests following the Wassermann type have been developed, using as antigen an alcoholic extract of cultures of *E. histolytica*. They are of use when the organism is suspected to be

present but has not been revealed by repeated examinations of the stool.[4] Others feel that the complement fixation test is of doubtful value.[17]

Sigmoidoscopy is employed by some to obtain smears from ulcers but frequently the ulcers may be so far up in the colon that the instrument will not reach it. In most cases where ulcers are within reach the parasite is almost certain to show up in the stool.

Prognosis

Adequate therapy usually effects a complete cure in cases of mild amebic colitis but if untreated the condition may continue for several years and may gradually grow worse and finally result in death. The mortality rate in treated cases is less than 5 per cent of those who contract the disease but is as high as 20 to 40 per cent in those not treated. If the condition has developed to the liver abscess stage the patient has a chance of survival directly dependent upon the number of abscesses, their location in regard to drainage, the presence or absence of a secondary bacterial infection and therapy with emetine before surgery.[21]

Therapy

General Measures

Various general measures are of value in the treatment of amebiasis. If diarrhea is one of the predominant symptoms along with fever and prostration absolute bed rest is indicated. Headache, neuralgia, intestinal discomfort and insomnia may be relieved by giving the following in capsule form as needed:[17]

Acetylsalicylic acid	0.12 Gm.
Acetophenetidin	0.2 Gm.
Belladonna extract	0.005 Gm.
Dihydromorphinone hydrochloride	0.002 Gm.
Phenobarbital	0.03 Gm.

Relief of insomnia and assurance of adequate rest also may be effected by administering one of the barbiturates.

If the bowel movements are too frequent the following may be given in powder form as necessary.[17]

Powdered opium	0.06 Gm.
Bismuth subcarbonate	0.5 Gm.

To control colic it may be necessary to give 8 cc. of paregoric every 2 hours. If the colic is severe it may be necessary to administer parenterally 8 mg. of morphine sulfate or 2 mg. of dihydromorphinone hydrochloride with 5 mg. of atropine sulfate.[13] Other drugs employed for this purpose also include a kaolin-pectin or kaolin-aluminum hydroxide mixture. Phenobarbital, atropine, codeine or an antispasmodic such as diphenylacteyldiethyl-aminoethanol hydrochloride also may be useful. Administration of the preceding prescrip-

Table I

CONDITION	THERAPY
Asymptomatic amebiasis	Diiodo-hydroxyquinoline Chiniofon Carbarsone Iodochlorohydroxyquinoline
Symptomatic amebiasis	Diiodo-hydroxyquinoline Chiniofon Carbarsone Iodochlorohydroxyquinoline Azosulfamide, if there is severe abdominal distress
Acute or Chronic Amebic Dysentery	Azosulfamide with diiodo-hydroxyquinoline, chiniofon, carbarsone or iodochlorohydroxyquinoline
Amebic hepatitis and liver abscess	Emetine and diiodo-hydroxyquinoline, chiniofon, carbarsone or iodochlorohydroxyquinoline Azosulfamide, if there is severe abdominal distress Aspiration Surgery
Amebic invasion of other organs	Emetine followed by diiodo-hydroxyquinoline or chiniofon

tion to control the diarrhea may result in a constipation for which some state that a cathartic can be given.[13] Others recommend a small enema of plain water when necessary and daily administration of 15 cc. of liquid petrolatum orally.[17] Still other authorities recommend that laxatives or constipating agents should not be used.[11]

In those cases with rectal ulceration accompanied by tenesmus the following prescription injected into the rectum in doses of 1 tablespoonful every 4 to 6 hours may be helpful:

Iodoform	10.0 Gm.
Olive oil	120.0 cc.

This should be stored at refrigeration temperatures.

Other medications more frequently employed for this therapy include analgesic, medicated suppositories and/or ointments such as those containing butyl aminobenzoate, ethyl aminobenzoate or diperodon. Sitz baths or sodium bicarbonate irrigations are also of value.

Diet

The diet is also important in the therapy of amebiasis and should be bland and supplemented with vitamins. In those patients where the condition is severe frequent feedings of boiled milk, stale or toasted white bread, white rice, gelatin, soft cooked eggs and tea are indicated.[13] Raw fruit and vegetables and other roughage should be avoided.

Alcohol is believed to be a predisposing factor to amebic hepatitis and liver abscess.[19] Other workers also recommend the avoidance of tobacco.[20]

Supplementary vitamins are indicated and the following capsule, taken before each meal, is recommended by some:[17]

Thiamine hydrochloride	5 mg.
Riboflavin	3 mg.
Nicotinic acid	25 mg.
Ascorbic acid	50 mg.

Some believe that this formula is not an adequate supplement and therefore advocate a high vitamin potency such as that contained in the therapeutic formulas.

Fluids

If the diarrhea is severe it is necessary to administer fluids so that the intake equals the output. If possible the fluids should be given orally but in some cases it may be necessary to give them intravenously or by hypodermoclysis. If given parenterally 5 per cent glucose in physiologic salt solution is indicated. The average amount necessary usually ranges from 2500 to 3000 cc. per day.[17, 21] One worker also reported that blood and plasma transfusions were useful.[21]

It is important in setting up the dietary regimen and general therapeutic measures that the severe diarrhea be treated, salt loss, dehydration, caloric deficit, avitaminosis, anemia and hypoproteinemia corrected.

Disinfection

Although the disease is spread chiefly by the convalescent patient or the chronic carrier of the cyst the excreta of the patient during the acute stages should be disinfected by adding chlorinated lime solution (½ lb. of chlorinated lime to a gallon of water), or a 5 per cent solution of phenol, compound cresol solution or sodium hypochlorite to the excreta before disposal. The bed linen and clothing should be boiled after each use. Nurses or other attendants should carefully cleanse their hands before going to other patients.[13]

Drugs

Specific drug therapy of amebiasis is directed toward the relief of symptoms by stopping the growth and invasion of the trophozoites in the tissues and also toward the prevention of transmission and reinfection by eradicating the cysts clinging to the bowel surface.

Prior to World War II, the drug therapy of amebiasis consisted of giving a combination of 2 of the specific drugs for a certain period of time along with emetine at the beginning in acute cases. If necessary this regimen was repeated at intervals with rest periods between. However, dur-

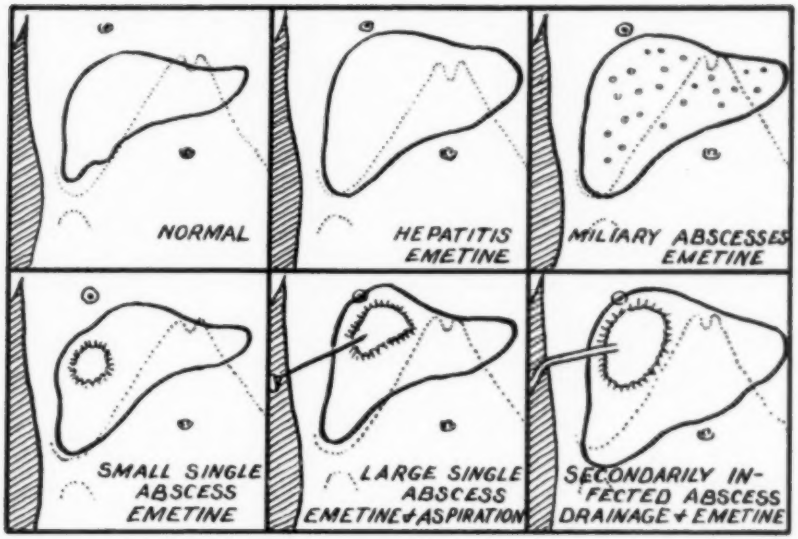

Fig. 4. Stages of liver involvement in amebic dysentery and treatment (according to Napier).

ing World War II it was found that certain cases did not respond to this therapy. One worker propounded the theory that some strains of amebae are more pathogenic than others but it is generally the consensus that this is not true. A study revealed that the refractory cases would respond to the combined therapy if it was begun early in the course of the disease.[22] Further investigations revealed that emetine alone is not sufficient to eliminate the infection; that an emetine-fastness may develop resulting in the organisms being less susceptible to other drugs also; that the refractory cases were all in a war zone and consequently were not given the detailed care which is necessary; that the patients were generally undernourished and debilitated; and that there were probably serious secondary infections present.[21, 23-25] Following these conclusions the Army adopted a routine for treatment.

Army Regimen

Course A, which was given in those acute cases in which the trophozoites were found in the stools, began with a daily hypodermic injection of emetine hydrochloride for 4 to 6 days. This was followed immediately by emetine-bismuth-iodide orally for 12 consecutive days. For the same 12 days chiniofon, in the form of a retention enema, was also given. For the next 12 days diiodo-hydroxyquinoline, carbarsone or acetarsone was given orally with the first drug preferred. The patient was allowed to rise during this period. Succinylsulfathiazole was given at the same time as the emetine in case bacillary dysentery also was present. Course B, given to carriers who had no symptoms of the disease, followed the same regimen with the omission of the emetine therapy. For refractory cases, resisting the routine treatment, (Course C) penicillin and succinylsulfathiazole were given first to eradicate the secondary pyogenic organisms. It was discovered that, although penicillin has very little if any effect on *E. histolytica* itself, it did relieve the symptoms and make the refractory chronic case more susceptible to routine therapy. Succinylsulfathiazole attacks certain other organisms which penicillin does not. If these 3 courses failed to bring about a cure a rest period of 10 to 12 days was indicated fol-

lowed by another course of therapy. The Army achieved rather satisfactory results with this regimen.

Emetine Hydrochloride, U.S.P.

Emetine hydrochloride is indicated in severe acute amebic dysentery, in acute exacerbations of chronic amebic dysentery and in amebic liver abscess and hepatitis. Studies have shown that no other drug stops the dysentery as quickly. Because emetine has no effect on the cysts it is not indicated in the therapy of carriers. Some feel that the effectiveness of emetine is considerably exaggerated and that it should be given only to relieve acute symptoms in the therapy of amebic hepatitis, amebic liver abscess, amebic granuloma and extra-intestinal amebiasis.[17] Recently there was reported a case which was suspected to be amebic pulmonary abscess but no positive diagnosis could be made. However, therapy with penicillin and sulfadiazine produced no therapeutic response. Intramuscular injection of 0.06 Gm. of emetine hydrochloride daily for 10 days resulted in a rapid response in the clearing of the abscess.[26] Emetine is given to adults in a dosage of 60 mg. or 1 gr. subcutaneously (or intragluteally) for 12 successive days.[17] Some advocate that it be given for no more than 10 days in succession.[12] Others recommend that it be given only long enough to control the dysenteric symptoms; in recurrent dysentery for 5 to 6 days and in liver abscess or hepatitis for 10 to 12 days.[11] The dosage, (subcutaneous administration) recommended for children by one authority is no more than 20 mg. per day for children over 8 years of age and no more than 10 mg. for younger children.[17] Some feel that it should not be given to children and others state that it should not be given to young children unless all other therapeutic measures have failed.[11, 17] A second course of emetine, if indicated, should not be given until 6 to 8 weeks have elapsed since the last course. Emetine is capable of curing only about 30 per cent of patients but it does relieve the symptoms in about 80 per cent. Emetine is generally administered parenterally although there are some objections to this method. Pain, discoloration of the skin and in rare cases sloughing of the skin follows the subcutaneous injection of this drug. Some prefer to inject the drug intramuscularly deep into the gluteal region because the pain and discoloration do not occur but absorption is more rapid by this route. If the patient is not sensitive to procaine a 1 to 2 per cent procaine hydrochloride solution can be used as the vehicle for the drug with the result that the pain of injection is eliminated. Considerable pain is caused when it is given in an enema. Although some have obtained results with the intravenous route[27] most workers consider this too dangerous. Preliminary work has been done on the possible oral administration of emetine. It was given in doses of 20 mg. in the form of enteric-coated tablets, 3 times a day for 12 days to one group and 40 mg. 3 times a day to another group with no serious reactions occurring.[27] However, further study is believed necessary.

Because emetine given alone will not eliminate the cysts from the lumen of the bowel and therefore allows recurrences, it is necessary to give an iodine or arsenical compound either simultaneously or following the course of emetine. If there are lesions in the lower colon or rectum which are not affected by this therapy it may be necessary to administer these drugs by retention enemas. Care should be taken that the enema is not given too high so as to cause damage in the bowel which is ulcerated. When emetine is given, the patient should be kept in bed and pulse and blood presure observed very carefully. If symptoms of toxicity appear, administration of the drug must be stopped at once. These toxic manifestations include nausea, vomiting, diarrhea, weakness, faintness, ankle, wrist or toe drop, fall in blood pressure, auricular fibrillation, cyanosis, dyspnea, mental depression, tachycardia, peripheral neuritis, desquamation of the skin, stiffness of the legs, muscular pains and sudden cardiac failure. In some studies it was thought that some of the reactions were due to an excessive dosage or to an idiosyncrasy to the drug.

Emetine should be given cautiously to pregnant women and is contraindicated in treating patients who have any cardiovascular disease or kidney or liver damage.[11, 13, 17, 27, 29-32]

In using emetine in treating amebic hepatitis and/or liver abscess the heart muscle should be checked by electrocardiogram prior to therapy and after the fifth day of therapy daily to see if there are any changes in the Q.R.S. complex and inversion of the T wave caused by the drug.[17]

Mention was made previously of the possibility of emetine fastness; however, the scientific evidence thus far assembled does not provide any proof of this.[25, 33]

Emetine and Bismuth Iodide, B.P.

Emetine and bismuth iodide is a complex iodide of emetine and bismuth which is official in the British Pharmacopoeia. It contains approximately 25 to 28 per cent of emetine and 18 to 21 per cent of bismuth. Because of its insolubility it was believed to be less irritating to the stomach. Slow decomposition of this product in the intestinal tract provides emetine for absorption. Most workers believe it to be less effective than the soluble salts given by injection but a report has been made that it possesses activity against the "free-swimming" forms which emetine by parenteral route does not have.[34] It is administered in doses of 60 mg. to 0.2 Gm. in pill, tablet or capsule form on an empty stomach before going to bed, for 12 consecutive days.[35] It is reported that the drug is best given in a gelatin capsule. To allay nausea a barbiturate also may be administered. The stools should be observed for a dark brown or black color which will indicate that the capsule has disintegrated.[13]

Chinofon U.S.P., N.N.R.

Chiniofon is a mixture of 7-iodo-8-hydroxyquinoline-5-sulfonic acid, its sodium salt and sodium bicarbonate and contains 26.5 to 29 per cent of iodine. This drug is absorbed, and through the bloodstream is able to act directly on the amebae invading the lumen of the bowel. It is capable of destroying both trophozoite and cyst forms of *E. histolytica* and therefore is of value in treating acute and chronic intestinal amebiasis. It is not effective in cases of liver abscess or hepatitis. Chiniofon is given orally or rectally but never intravenously. The oral dosage recommended for adults is 0.25 to 1.0 Gm. in pills, tablet, cachet or solution form 3 times a day for 7 to 14 days.[36] Others recommend a dosage of 1 Gm. 3 times a day for 7 consecutive days followed by a rest period of 3 to 4 days and then a course of the drug for 3 to 7 days.[17] The dosage for children is dependent upon the age according to some.[36] Others recommend a dosage of .065 Gm. (1gr.) per lb. of body weight 3 times a day. When given with emetine these same dosages are used. In patients with heart conditions, who cannot take emetine, chiniofon may be used in doses of 0.5 Gm. 3 times a day after meals until a total dosage of 25 Gm. has been given.[17]

In cases of mild amebic colitis the oral dosage recommended is 0.5 to 0.75 Gm. 3 times daily for 8 to 10 days.[11]

Chiniofon is also given rectally. In the emetine course of therapy a cleansing enema of hot water is followed by a retention enema of 3.0 Gm. of chiniofon in 300 cc. of sterile water.[17] In acute cases or in serious chronic cases with obstinate clinical symptoms chiniofon may be given both orally and rectally. The dosage rectally which is recommended is 1 to 5 Gm. in 200 cc. of water at a temperature no higher than 45°C. Some state that chiniofon is first given as an enema consisting of 200 cc. of a 2.5 per cent solution and if well tolerated the strength and quantity are increased until a series of 12 on consecutive days have been given. One worker[35] suggests that the foot of the bed be raised on 8-inch blocks and that the patient lie for a half hour each on his right side, back and left side as an aid to retaining the enema but the value of this is questioned by others.[13]

Although chiniofon has not been observed to cause any severe toxic reactions like emetine it may cause abdominal colic or diarrhea which may make it necessary

to reduce the dosage or discontinue the drug altogether. It has been suggested that the diarrhea which may develop on the second or third day of the course of therapy may be controlled by giving 8.0 cc. of camphorated tincture of opium or 12 to 24 cc. of an aluminum hydroxide gel with kaolin (20 Gm. per 100 cc.) after each bowel movement.[17] One authority has stated that because of the development of this diarrhea chiniofon cannot be given for longer than 10 days.[12] It has been reported that oral administration of chiniofon causes a scalding sensation while the patient defecates and for this reason it is not used so frequently as in the past.[13] This statement does not appear to be in agreement with that of other workers.

In cases of amebiasis where there is liver damage chiniofon should be used cautiously until further studies have been made in this respect. If there is a thyroid disturbance the iodine content of chiniofon should be carefully considered.[36] Administration of chiniofon is believed to result in cures of 90 per cent of the patients treated.

Diiodo-hydroxyquinoline N.N.R.

Diiodo-hydroxyquinoline contains 60.5 to 64.0 per cent of iodine. It is indicated in the therapy of amebic dysentery, asymptomatic intestinal amebiasis and carriers. Because of its relative insolubility diiodo-hydroxyquinoline is less likely to irritate the intestine, and to cause toxic reactions. As a result it can be given over longer periods of time. One authority has stated that this drug can be given over a 20 day period.[12] The recommended dosage of diiodo-hydroxyquinoline is 1.47 to 2.1 Gm. daily for 15 to 20 days.[17, 36] An other worker recommends a dosage of 0.63 Gm. 3 times a day for 20 days.[11] Other dosages used particularly when following the emetime and chiniofon course include that of 0.2 Gm. 3 times a day for 20 days. The dosage for children is calculated according to 0.21 Gm. per 15 lbs. of body weight. Children of 6 to 11 years are sometimes given two-thirds of the adult dose.[37] Some report that no toxic reactions or contraindications have been observed for diiodo-hydroxyquinoline. Others have found abdominal pain, diarrhea and headache[38] and others dermatoses attributable to the drug.[39, 40] Although a course of chiniofon followed by diiodo-hydroxyquinoline will generally cure 70 per cent of the symptomatic cases with one course or series[12] it may be necessary to repeat the course in which case there should be a rest period of one week. Hospitalization will not be necessary usually unless the case is very severe. It has been stated that diiodo-hydroxyquinoline is 85 to 90 per cent effective.

Iodochlorohydroxyquinoline, N.F., N.N.R.

Iodochlorohydroxyquinoline contains 38 to 41.5 per cent of iodine and 11.4 to 12.2 per cent of chlorine. It is indicated in the therapy of chronic and acute intestinal amebiasis. It finds particular usefulness in oral therapy of ambulatory carriers.[17] The recommended oral dosage is 0.75 to 1.0 Gm. each day given in divided doses of 0.25 Gm. for 10 days. Others report use of a dosage of 0.5 Gm. twice a day for 10 days.[13] If it is necessary to repeat the course a rest period of a week to 10 days should be observed.[37] For children the dosage indicated is 0.02 Gm. per 15 lbs. of body weight, 3 times a day.[17] Some state that this drug should not be used rectally whereas others have used 200 cc. of a 1 per cent suspension of the powder for 5 doses on alternate nights with no evidence of irritation.[41] Iodochlorohydroxyquinoline is more toxic than chiniofon but less so than carbarsone. Some gastrointestinal irritation has been reported following the dosage described. Iodism may be a possibility as well.[36] Other toxic symptoms which have been observed include abdominal colic, flatulence, mucoid and bloody stools, headache and palpitation. After administration of the drug for 2 or 3 days diarrhea may develop as occurs with chiniofon. The control of this condition is the same as previously described.[17] If there is liver damage this drug should be used cautiously until further evidence has been presented on this phase.[36] Excellent results were obtained with this drug

in treating patients from the Pacific theater of World War II.[41] Iodochlorohydroxyquinoline is reported as being effective in 80 per cent of cases treated.[17]

Acetarsone, N.F., N.N.R.

Acetarsone has shown some favorable effects in amebiasis therapy. It contains 26.9 to 27.6 per cent of arsenic. The dosage recommended for adults is 0.25 Gm. orally 2 or 3 times a day for 7 days. Generally this drug is employed following a course of emetine. Because it is a rather toxic arsenical the patient must be watched carefully for gastro-intestinal symptoms and hepatitis as well as various cutaneous disturbances such as urticaria, erythema and hemorrhagic eruptions.

Carbarsone, U.S.P., N.N.R.

Carbarsone contains 28.1 to 28.8 per cent arsenic and of the arsenicals is the one used more frequently. It is considered to be the most efficient drug which can be used alone in treating intestinal amebiasis.[17] However, some workers believe that it should not be used unless the hydroxyquinolines are not available. Carbarsone is particularly indicated in the therapy of the chronic asymptomatic type of amebiasis. It is administered alone or for greater effect following a course of emetine therapy. Orally the recommended dosage is 0.25 Gm. twice daily for 10 days.[36] Some suggest that this dosage be given three times daily for 7 days.[11] Others report giving this dosage twice a day for 12 days.[13] The daily dosage for children is based on .065 Gm. per 20 lbs. of body weight. For best results the drug should be given following the morning and evening meals. Carbarsone is also administered rectally and may be used in this fashion to supplement a course of emetine as mentioned previously. If used following emetine or alone the dosage is 2.0 Gm. in 200 cc. of a 2 per cent sodium bicarbonate solution given as a retention enema for 5 alternate nights after cleansing with an alkaline enema.[36] Some workers suggest that the drug be given for 5 consecutive nights unless it becomes irritating in which case it should then be given on alternate nights.[17] If the enema is expelled before morning it is suggested that the therapy be repeated on alternate evenings until 5 enemas have been retained all night.[13] A mild sedative such as 0.2 Gm. of monosodium isoamylethylbarbiturate may be helpful to the patient in retaining the enema. The drug should not be given orally and rectally at the same time because the rectal dose is quite large. Rectal administration is particularly indicated if there are lesions in the lower colon or rectum, in acute amebic dysentery or in resistant cases in which the stools contain motile amebae. Carbarsone appears to be less toxic than acetarsone but it may cause toxic reactions which necessitate a reduction in the dosage or stopping the drug entirely. Such reactions include abdominal distress, diarrhea, nausea, vomiting, abdominal colic, jaundice, neuritis, pruritus, cutaneous disturbances commonly caused by arsenicals and rarely visual disturbances caused by injury of the optic nerve. Carbarsone is contraindicated in patients with amebic hepatitis, kidney disease or who are sensitive to arsenic. It is reported to be effective in 90 per cent of cases treated.[11, 13, 17, 36]

Azosulfamide

In certain selected cases azosulfamide is given in conjunction with diiodohydroxyquinoline or chiniofon to adults in doses of .065 to 0.195 Gm. 3 times a day for 5 to 7 days. The dosage for children is calculated on the basis of .065 Gm. per 10 lbs. of body weight 3 times a day. Because of the toxic nature of the drug it should be discontinued as soon as relief of abdominal distress occurs. This drug, in conjunction with one of the hydroxyquinolines, has been found to relieve the symptoms promptly and effectively and cause permanent cure in 50 per cent of patients so treated.

Trilactic

Trilactic is an anhydrous form of lactic acid which is being investigated for its value in amebiasis therapy. Thus far

good results have been reported in treating acute amebiasis with dysentery and chronic amebiasis without dysentery, particularly when this new drug is given in conjunction with one of the iodine compounds. Its effectiveness is believed to be due to a reduction of the pH of the large intestine resulting in an unfavorable environment for the reproduction process of the ameba thus enhancing the amebicidal action of the iodine preparation. The dosage used in acute amebiasis with dysentery is 40 to 50 Gm. given in 4 divided doses in pulverized rice or semifluid oatmeal daily for 7 days after which the dosage is gradually reduced, particularly if the acute stage has been stopped. In cases of chronic amebiasis without dysentery the dosage used is 3 tablespoonfuls daily divided into two doses morning and night. Thus far no reports of toxic effects have been made.[12]

Chloroquine Diphosphate

Chloroquine diphosphate, although chiefly of value in malaria, has shown usefulness in amebiasis, particularly in amebic hepatitis. Examination has shown that 400 times as much of this compound is found in the liver as in the blood after its administration. In the safe dosage employed it has been found to cure liver abscesses. It is relatively nontoxic. Further investigations are being carried out with this compound in this respect because thus far emetine is the only drug which has eradicated liver abscess, and it does have a deleterious effect on the heart.[12]

Recent announcement was made of two new compounds which are being tested for use in amebiasis. One compound, known as bismuthoxy-*p*-N-glycolylarsanilate (15.7 per cent arsenic and 37 per cent bismuth), when given to 31 patients, promptly eliminated the infection and resulted in permanent cures in 28. Relatively large doses could be given for 7 to 10 days. In another study of this compound 68 cases of chronic and subacute intestinal amebiasis were treated with oral doses of 0.5 Gm. after each meal for 7 days. The dosage given to children was reduced proportionally according to weight. A number of other cases were also given chiniofon and/or bismuth subgallate and 32 control cases were treated with chiniofon alone. The latter drug was given in doses of 0.25 Gm. with a total dosage of 11.25 Gm. given in 7 days. The bismuthoxy-*p*-N-glycolylarsanilate alone cleared 24 out of 25 cases without relapse; chiniofon alone cleared only 5 out of 11 cases. The two drugs in combination or given alternately effected clearance in 33 of 38 cases. Five out of 5 cases were cleared when the bismuthoxy-*p*-N-glycolylarsanilate and bismuth subgallate were given alternately. No side effects were noted when this new drug was given and therapeutic response was prompt.[41] The second drug being tested is related to chloroquine in that the structure is identical but iodine replaces the chlorine. This results in slower absorption and increased activity against amebae. Thus far experimental animals given the drug have been freed of the amebae in the intestines.

Conessine

The use of conessine hydrochloride or hydrobromide in amebiasis therapy has been reported in France. Several courses of emetine were given to 42 patients with acute amebiasis with no response in 39 of the subjects. When all 42 were given the conessine drug there was rapid general improvement and prompt return to normal of the number and volume of stools. Only 2 patients, in whom therapy was stopped prematurely, did not show complete sterilization. Instrument examination revealed that the ulcerations were healing or the mucosa was improving. Two cases of acute hepatitis were treated with similar results but there were rapid recurrences.[42]

In another study 12 patients with chronic intestinal amebiasis following oral administration of 0.3 to 0.4 Gm. of conessine hydrochloride daily until a total of 2.4 Gm. were given in 6 to 8 days, showed normal stools and disappearance of clinical symptoms. One patient, given 0.75 Gm. subcutaneously and 1 Gm. orally, relapsed but was cured by giving 0.2 Gm. daily for 8 days. A dosage of 0.1 Gm. three times

daily for 1 week cured a patient who had resisted all other therapy. Another patient having both amebae and trichomonads was also successfully treated and both parasites disappeared. In a second group of 12 patients oral doses of 0.5 Gm. daily up to total doses of 5 to 5.5 Gm. in 5 to 6 days were effective in relieving pain and tenesmus in 48 hours and in eliminating the parasite in 7 of the 12. Side effects observed included insomnia, disorientation, tremors, vertigo, tinnitus and salivation.[42a]

Chemotherapeutic Measures

Amebiasis may be complicated by a secondary bacterial infection and in order to eliminate this possibility some recommend that amebicidal therapy be preceded or followed by penicillin. The dosage recommended is 100,000 units first and then 30,000 units every 3 hours until a total of 2,000,000 units is reached. In order to eradicate or reduce the number of Gram-negative organisms which are not affected by penicillin, succinylsulfathiazole is given in oral doses of 20 Gm. daily. In this respect sulfaguanidine or phthalylsulfathiazole may be employed instead of succinylsulfathiazole.[12, 17]

Therapy of Complications

The more severe forms of amebiasis result in amebic hepatitis or liver abscess. In such cases a course of emetine and an iodine or arsenical compound is indicated.

If this fails to relieve the symptoms in 2 or 3 days it is necessary to aspirate the area.[11] Some recommend that the emetine be given the full time to act since it has been found that aspiration may be avoided unless the symptoms are such that it must be done immediately.[13] In this event the puncture should be made at the site where intercostal tenderness is at a maximum or if this cannot be determined then in the ninth right intercostal space in the anterior axillary line. In performing the aspiration rigid aseptic technic must be observed. A needle of large bore should be inserted no farther than 2½ inches. In some cases the process may have to be repeated.[11]

Emetine and aspiration have largely replaced surgical drainage and even aspiration may be avoided if emetine is given an adequate chance. Recent reports have verified this. In a series of 63 cases 19 (3 with hepaticobronchial fistula) recovered from emetine therapy alone; 18 recovered following emetine therapy and then aspiration; of 26 treated by open surgical drainage, with or without a prior emetine course, 14 died.[43] A series of 69 cases was treated with emetine alone and 68 recovered.[44] In 83 cases only 3.6 per cent died following emetine therapy with or without aspiration whereas 22.1 per cent died when surgical drainage was done.[45] However, if there is a secondary infection, multiple abscesses or left lobe abscesses surgical drainage may be indicated but in no case should it be performed unless emetine has been given first or is given simultaneously.[11,13] It has been recommended by others that surgical drainage be used only in those cases in which acute perforation into the peritoneum or pleura has occurred or is about to occur or when there definitely is a pyogenic infection present.[46] The patient's condition governs whether complete rest or immediate surgery is indicated in cases of peritonitis, perforation or severe bowel hemorrhage.[13] Emetine and the usual therapy for abscesses of the lung and brain are usually successful in these conditions since the vegetative forms of amebae are generally involved rather than the cysts. Penicillin has been found to control secondary infection with hemolytic streptococcus in the cavity along with hepatic abscess. Emetine and aspiration were not successful. In one case a total of 830,000 units of penicillin was given in 15½ days in dosages of 25,000 units for 8 doses every 4 hours, then 10,000 units for all doses for 7 days, and finally 5,000 units. It was believed that smaller dosages with occasional aspiration might have been just as successful.[47] In another case penicillin eradicated the secondary infection which developed after a rib resection for empyema and also eliminated the amebae from the purulent fluid.[48]

The other drugs described previously

should not be administered in cases of known liver abscess until the liver involvement has subsided following emetine therapy with or without aspiration because they do have possible toxic reactions on the liver.

Effectiveness of Therapy

Amebiasis is a relapsing disease and therefore the effectiveness of therapy should be judged by microscopic examination of the stools during the course of treatment. Some recommend that a period of 2 weeks should be allowed to lapse after completion of therapy and then a stool on 6 consecutive days should be examined microscopically. As a test of cure a sigmoidoscopic examination should then be made. This is the procedure followed by the Army.[13] Others recommend the examination of 3 stools passed on successive days and then 3 stools at intervals of a month and others recommend this be done for at least 3 months after treatment.[11, 49] This applies to patients and carriers. In amebic carriers without dysentery some recommend that 7 days after therapy is completed the stools be examined for cysts on 3 consecutive days, then once a week. After 3 months the stools from 3 consecutive days should again be examined.

Repetition of Therapy

In some cases the tests will reveal that amebae are still present at the end of a course of therapy or the symptoms may recur before the rest period is over. In this event another course is begun. In the Army regimen described a course involves 30 days and with the two week rest period before testing for cure over 40 days have passed so that it is considered safe to repeat the course immediately. If symptoms still persist at the end of the 30 days of therapy many resume treatment at once. A series of cases of hepatic amebiasis which resisted therapy with doses of 0.39 Gm. of emetine were found to improve after a rest period of 2 weeks followed by another course. Improvement in some instances continued for as long as 2 weeks after discontinuing therapy. Cumulative toxic effects were thus avoided. However, it was also reported that the rest period should not be extended beyond 2 weeks in cases where there was liver tenderness, leukocytosis or increased sedimentation rate because clinical recrudescence was then a possibility. This worker found no toxic effects when he gave the second and third courses with rest periods of only 8 to 10 days in some more acute cases.[44]

Prophylaxis

Prophylaxis against amebiasis may be accomplished in various ways. Proper water purification and sewage disposal are important factors but there are many areas in the world which are not sanitary.Contaminated drinking water is very common in such areas. It is necessry to treat such water by special filtration, or chemically, so that residual chlorine will be present in a concentration of 1 part per million after 30 minutes.[5] Too often this is not done because the facilities are not available. Therefore the individual who travels or spends some time in these areas should take certain precautions. If possible food and water supplies should be protected from contamination. This can generally be done but the individual cannot always accomplish complete protection because of food handlers and other individuals involved. Therefore it is wise to avoid all water which has not been previously boiled and all food which is not thoroughly cooked. Raw fruits and vegetables should be avoided unless they are the type which can be peeled just prior to eating. Salads are frequently at fault as sources of infection. Contact with flies should be kept at a minimum. Thus far none of the drugs described has proven satisfactory as a prophylactic agent for inhabitants of areas where amebiasis is endemic but for those who are passing through or staying for a short time diiodo-hydroxyquinoline is of some value. Some recommend the same dosage as for therapy, and that it be taken for 20 days even though the individual does not remain in the endemic

area that long. If he remains longer another course may be taken after a rest period of one week.[13] Others recommend a dosage of 0.42 Gm. twice a day for 30 days or more;[11] or 0.42 Gm. 3 times a day for 20 days.

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Multiple Sclerosis

General Consideration

Arthur J. Schwenkenberg, M.D.
Dallas, Texas

There is an important and large group of diseases of the central nervous system classified as the Demyelinating Diseases—so called because the pathology is a focal or diffuse disturbance of the myelin sheaths (white matter) of the nerve fibers in various regions of the nervous system, and to a lesser degree affecting the neurones or their processes. The early pathology in these diseases is a destruction of the myelin with varying sized patchy sclerosis, with tendencies toward fluctuations, remissions and exacerbations. Eventually the demyelination is followed by gliosis. Sometimes the gray matter in the cerebral cortex may be affected; rarely is the gray matter in the spinal cord affected.

The etiology of this group of diseases is generally not too well known—if known at all. The different forms which can aptly be described are (1) acute disseminated encephalomyelitis, or simply acute encephalomyelitis; (2) disseminated myelitis with optic neuritis; (3) diffuse sclerosis, and (4) acute disseminated encephalomyelitis which not infrequently follows vaccination and acute infectious diseases such as measles, chickenpox and rabies. Another form, the most common and the one in which I am chiefly interested here, is disseminated or insular sclerosis, also known to all of us since our medical school days as Multiple Sclerosis, which term for practical purposes serves best to describe this mysterious disease.

It has been repeatedly suggested that perhaps all these diseases are one and the same, varying only in intensity and in time. Some, however, have a definite familial tendency (Schilder's disease and Krabbe's Disease, etc.), quite apart from the post-infectious varieties, whereas Multiple Sclerosis has some fairly distinctive features as to age incidence, geographic distribution, clinical behavior, personality changes, and especially the tendency toward remission or acute exacerbations.

Multiple Sclerosis has interested investigators for years. The Association for Research in Nervous and Mental Disease devoted its discussion at their annual meeting in 1921 to Multiple Sclerosis. At this Association's annual meeting of 1948, Multiple Sclerosis was again the topic for discussion. A National Multiple Sclerosis Society for the advancement of research on Multiple Sclerosis, with headquarters in the Academy of Medicine Building in New York City, was organized some two or three years ago and many patients with this disease are registered with the Association.

There appears to be some promise regarding an explanation of the unknown etiology of Multiple Sclerosis. Dr. Tracy J. Putnam, some time ago, pointed out the possible cause to be due to thrombosis of veins or venules near the demyelinating foci. Other investigators have also centered their attention upon circulatory phenomena —arteriole spasm or enzymes emanating from the blood. There are many who still feel that Multiple Sclerosis is due to a virus infection or toxic state and is merely one form of Disseminated Encephalomyelitis.

The geographical distribution of Multiple Sclerosis is of interest, and particularly to me here in the Southwestern part of the United States where I have seen cases consistently for the past twenty-four years. Multiple Sclerosis is considered to be a disease of Northern countries and is prevalent in Northern Europe, Switzerland, the British Isles, and the Northern United States, especially in New York and the Great Lakes regions. The disease is considered rare in China, the tropics, and

the South and Southwestern part of the United States.

At the meeting of the Association for Research in Nervous and Mental Disease in 1921, a statistical survey for geographical distribution indicated that no cases were found in Texas among the draftees of World War I. It was interesting to me in October 1924, after returning to Texas from New York, that the first neurological case referred to me was the cousin of a classmate. This female presented a classical case of early Multiple Sclerosis (case report below), which diagnosis was later confirmed by Dr. Edwin G. Zabriskie at the Neurological Institute in New York. This patient is still living although she has been a confirmed invalid for years. Some months later, a young dentist whom I consulted told me that only a few months before he had experienced diplopia, and had had some difficulty with his left leg. Neurological examination at that time revealed only a suggestive Babinski on the left and a slight increase in the deep reflexes. This man some ten years later, following an influenza infection, developed a classical Multiple Sclerosis and also spent some time in the New York Neurological Institute. He recently died. The third case and even more interesting to me was a fellow roommate who was with me in New York during our intern years and who afterward returned to his home in West Texas to practice medicine. He came to me about eight years ago complaining of ataxia. Neurological examination revealed a bilateral horizontal nystagmus and a definite pyramidal tract sign in the lower extremities. He has now been practically bedridden for three years.

It is possible that Multiple Sclerosis was not recognized in many areas of the country about the time of World War I because of the lack of neurological knowledge. It has also been thought that exacerbations in Multiple Sclerosis are not so severe in the Southwestern climate. I know of patients with Multiple Sclerosis who have been sent to the Southwest and to the Valley regions of Texas because of the belief that such a climate is beneficial. Recently, one quite advanced case came to Dallas, chiefly for climatic reasons. She died rather suddenly from genito-urinary complications only a few days ago. Another case just seen in the past week, also quite advanced, is now making arrangements to move to Texas.

Multiple Sclerosis occurs chiefly in younger individuals between the ages of twenty and forty. There are, however, cases reported after forty, although I feel there is a possibility that the disease may have begun during the earlier years, and perhaps had unrecognized fleeting symptoms only to reappear later as well advanced Multiple Sclerosis. Some investigators state that women are affected more than men, in proportion 3 to 2. Others report just the opposite. Occupation or social strata do not seem to have any particular bearing on the occurrence of the disease.

Clinical Behavior and Types

The principal sites are (1) the cerebral (2) brain stem and cerebellum, and (3) spinal cord. Dr. Richard M. Brickner, writing in a recent issue of the *Medical Clinics of North America,* describes four clinical types; i.e.:

(1) That with outbursts (attacks) and remissions;

(2) The chronic progressive type ranks next in frequency, followed by

(3) The stationary type,

(4) The acute type (acuteness of onset of a massive array of disturbances.)

The initiating factors, as well as factors precipitating attacks, have consistently been noted. Chiefly among them are *fatigue, cold, allergy, pregnancy and trauma.* In many instances, emotional stress has been observed. In other instances, nutritional factors and infectious diseases appear to have quite a prominent part to play.

Symptomatology

The outstanding symptomatology is a fluctuating course with a tendency toward remissions and exacerbations, with early symptoms resulting from involvement of the optic nerve (retrobular neuritis), and

often associated extra-ocular palsies (diplopia). Also frequently associated with these visual disturbances are monoplegias, hemipareses and even hemiplegias. Ataxia, sensory symptoms (numbness and tingling), early speech disturbances and bladder dysfunction may be noted. Dr. Brickner mentions the "signal symptoms" which often may be brought out in the history, in that the patient will frequently recall such fleeting symptoms months or years before. This is very important to develop in obtaining the history.

The majority of these patients by reason of their visual disturbances complain of misty vision, especially in one eye. Sometimes they describe what are field defects (half vision or inability to see to the side). As a consequence, they usually seek advice from an ophthalmologist. In instances where bladder dysfunction is early, they usually seek help from a urologist, whereas the monoplegias or hemipareses are described by them as "light strokes."

The symptomatology may be diveded into early and late. The early symptomatology is often fleeting or at least followed by remissions, whereas the late symptoms are more fixed and progressive, and usually the disabilities are greater, particularly the spasticity in the extremities, either monoplegic, hemiplegic or paraplegic distribution.

It must be kept in mind that the objective neurological findings, because of the diffuseness of the disease, are not confined only to the optic nerve. When one thinks of Multiple Sclerosis one usually thinks of the so-called Charcot triad (nystagmus, scanning speech and intention tremor). This triad, although considered quite pathognomonic of Multiple Sclerosis, is not always present and when it is it is usually seen in advanced or chronic cases. Common, however, are such signs as bilateral horizontal nystagmus, visual scotoma, absent abdominal reflexes, and increased deep reflex activity with spasticity. Often a unilateral or bilateral Babinski sign, as well as ataxia of the cerebellar type, can be early demonstrated. Sensory changes are infrequent and when they do occur they are largely subjective. On the other hand, symptoms due to the involvement of cerebellar spinal pathways, manifested especially by dysmetria, pass pointing, etc., are not uncommon. In a special article written by the National Multiple Sclerosis Society and appearing in the November 1, 1947 *Journal of the American Medical Association,* concerning chiefly diagnosis and treatment of Multiple Sclerosis, it is interesting to note the symptoms and signs enumerated in their order and the frequency of their occurrence in 141 cases, (male 77, female 64). This report points out that abdominal reflexes have been diminished in 83.7 per cent; nystagmus 70 per cent, Babinski sign present bilaterally 67 per cent; pupillary disturbances were rare; mental changes were noted in 15.8 per cent.

Mental and personality changes are of importance since generally these patients present a mild degree of, or at least a relative, euphoria. On the other hand, some cases have been reported to be depressed and even suicidal. Generally, one can expect the Multiple Sclerotic patient to be fairly pleasant and agreeable, cooperative, giving the impression that he is not too concerned about his illness; at least seldom giving any indication that he realizes the seriousness of it.

Diagnosis

The diagnosis of Multiple Sclerosis should not be difficult if one keeps in mind especially the age incidence, the tendency toward early visual disturbance often associated with mild pyramidal tract symptoms, or ataxia, with a history suggesting previous mild transitory symptoms. Then again, the tendency toward remissions and later exacerbations should always suggest Multiple Sclerosis. Hysteria must always be kept in mind, especially in the early phases, whereas in some of the later stages, particularly when the objective findings suggest spinal cord involvement, the possibility of subacute combined sclerosis, neurosyphilis or even a spinal cord tumor is to be considered. Amyotrophic lateral sclerosis should offer no difficulty because in this disease symptoms with reference to the anterior horn (localized atrophy,

muscle fibrillations), as well as definite pyramidal tract signs, make an early appearance. Furthermore, the other various demyelinating diseases must always be considered, but usually offer no great difficulty.

Laboratory diagnosis is of little assistance except for slight changes in the spinal fluid. In the early stages there may be a slight rise in the cell count, seldom more than twenty-five or thirty. The total protein usually is slightly elevated and occasionally there may be a change in the colloidal gold curve, even one approaching a paretic or syphilitic type. These changes in the colloidal gold curve, however, are rare.

Treatment

Through the years many different treatments have been tried, the majority merely on theoretical or empirical grounds. For many years, various forms of arsenical preparations, including silver-salvarsan and sodium cacodylate, were thought to be efficacious. Iodide, especially sodium iodide alone or combined with sodium salicylate, or glucose (intravenously), had its use. Fever therapy in different forms had its day. With the advent of vitamins, vitamin therapy has also been used very extensively. Following the research of Dr. Tracy Putnam and his theories regarding venous thrombi, an attempt has been made to treat Multiple Sclerosis by means of anticoagulants, particularly dicoumarin. The vasodilators, especially histamine acid phosphate, are still in an early experimental stage. Among such drugs now used are aminophylline, "syntropan" N.N.R., and papaverine hydrochloride in tolerance doses. Histamine acid phosphate, according to various reports and also in our hands, appears to offer encouragement although its use is still in very early experimental stages. The difficulty arising with the treatment in the early stages of Multiple Sclerosis is the fact that spontaneous remissions so readily occur it is often impossible to know whether the remission is the result of the treatment or whether it is spontaneous.

Other drug treatment directed chiefly toward relieving the spasticity is the use of curare, as well as neostigmine. Drugs such as amphetamine, benadryl, and a combination of these, have also been suggested, particularly in chronic cases. Recently E. R. Squibb & Sons have produced a formula (3-ortho-toloxy-1, 2- propanediol) known as Tolserol (known in England as Myanesin and studied there), which is now under investigation in this country.

In the treatment of Multiple Sclerosis the general hygiene, the avoidance of the precipitating factors mentioned above, as well as attention to the emotional and psychological effects, must always be kept in mind.

Physical therapy, in an effort to reduce spasticity and promote general improvement of the muscles, as well as prostigmine combined with curare, has its place.

Most neurologists, including myself, have run the gamut of various therapies; however, just recently we have been using the "histamine treatment", a procedure which was employed by the Mayo Clinic and reported in the article written by the National Multiple Sclerosis Association appearing in the November 1, 1947, *Journal of the American Medical Association*. Since then, we have treated seven cases and we have felt very much encouraged by the results. These cases are now under observation, reference being made to them in the series of cases presented below. Other cases are being treated.

I feel, if it is possible, that the vasodilators, particularly the histamine acid phosphate, should be used early. It is for this reason that Multiple Sclerosis should be recognized in the beginning and the early transitory and fleeting symptoms should be located, for many of these symptoms could easily be passed over as hysteria.

Although in our small series of cases, we have been following the "histamine treatment," as outlined in the article written by the National Multiple Sclerosis Society, appearing in the November 1, 1947 *Journal of the American Medical Association,* we are aware that other investigators are using different techniques, some giving larger doses of histamine acid phosphate and much more rapidly. We also

have used prostigmine bromide, curare and atropine sulfate, and recently have been trying some of the cases on Tolserol (Squibb).

The following cases have been picked at random from a fairly large series and are presented here merely to demonstrate some of the clinical features of Multiple Sclerosis. Incidentally, all of these cases were residents of Texas. Some of them have received the "histamine treatment" with fairly encouraging results. The cases are not presented in detail in order to conserve space:

Case 1:

Miss E. C. White female, AGE 19. Examined October 1924. Chief complaints: Fatigue, shaking of the hands and especially inability to strike the proper key on the piano. (She was a music teacher). She stated she had suffered from excessive fatigue since early in the spring and at that time she had difficulty with the vision in one of her eyes. She saw an ophthalmologist who suspected syphilis since her father had died with this disease. The visual disturbance, however, had improved considerably, but it was not corrected by glasses and she had a definite scotoma in the right eye. The outstanding neurological findings were a definite dysmetria in the right upper extremity, an increase in the deep reflexes on the right, absent abdominal reflexes. Later a positive Babinski was noted on the left. She was later examined at the Neurological Institute in New York and the diagnosis of Multiple Sclerosis was confirmed. This patient has received every form of treatment used during the past twenty years, but she never actually had a complte remission and has gradually become worse. For the past four years she has been a complete invalid because of a spastic quadriplegia. (She lives in a specially built chair). Her personality has been very pleasant and she continues to have hope. She keeps up with everything with reference to Multiple Sclerosis. During the past year she felt she had received some relief from prostigmine bromide. She has taken B-complex for several years. Recently she has had a little difficulty with swallowing. At no time has there ever been an exacerbation of her visual symptoms. Only in recent years has a slight bilateral nystagmus developed.

Case 2:

D. R. White male, AGE 17. Examined September 1938. Chief complaints: Double vision; eyes crossed; numbness of lip; difficulty in opening mouth and swallowing. History was to the effect that on July 17, he noticed a disturbance in sense perception in right hand which within the course of a few days extended up the arm and then into the right leg, especially around the right thigh. Some two weeks later, he noticed the same sensation in the left hand and left foot. About thirty days after the onset, he noticed numbness in the lips, first on the left and then on the right. After the numbness developed in the lips, the sensation in the extremity disappeared, and it was then, about September 1, he noticed double vision. Two weeks before I examined him his eyes were crossed. Objective neurological findings were weakness of the left (6th) cranial nerve, slight nystagmus to the right. No definite sensory disturbance involving either of the 5th cranial nerve distributions although he had some difficulty in opening the mouth. Deep reflexes were slightly increased on the right as compared to the left. No Babinski. Abdominal reflexes just barely elicited. In October after receiving an intensive course of sodium iodide and sodium salicylate, he was entirely free of visual symptoms except that the nystagmus was more pronounced, both to the right and to the left. The next time he was heard from was June of 1943, when I received a letter from an Army Base Hospital, Amarillo, Texas, inquiring about his past history. There was some question in the minds of those who examined him there whether his condition was that of Multiple Sclerosis or postencephalitis. Later he was discharged from the Service. I saw him again late in 1943. The nystagmus was very pronounced and he had an intensive tremor of the right upper extremity. Abdominal reflexes were still present, but very sluggish. There also was a questionable weakness of the left side of the mouth. He was in unusually good spirits and always presented a very pleasant personality. He was seen again in September 1944. The nystagmus was still present, but the abdominal reflexes were very active and there was still no evidence of a Babinski. The last time I saw him was in March 1946, and his condition remained unchanged except that he was having some difficulty adjusting himself in college.

Case 3:

Mrs. R. E. M. White female, AGE 23. Examined January 1947. Chief complaints: Weakness in right ankle, loss of balance, inability to write, generalized weakness, inability to walk without assistance, and visual disturbance. The history was to the effect that in November of 1943 the patient began having trobule with her right ankle turning and apparently for no cause; she described it as "just a weakness"—often she had to sit down and sometimes nearly fell. About the same time, she was having trouble with her eyes—"saw double"; diplopia came and went; also she had a numbness in her right hand and could not hold objects in it; at times had the same numb feeling in the right side of her abdomen. In 1944, her right ankle became even weaker. She was examined in February 1944 and was diagnosed as Multiple Sclerosis and braces placed on her leg which she wore for a while. Spinal fluid examination was also made

at that time. Since then her walking has become more difficult; she says that she "just folds up in the middle". For a while she had to be carried everywhere and could not even turn in bed. Patient was bedridden in the summer of 1945. She seemed to have no control of her body; she could write, but not legibly. She never complained of any pain. She got a wheel chair in December of 1945 and was able to use this without help. She has had no sense of balance since about the time she went to the hospital in 1945. Since that time she has improved gradually until now she can write, she also paints, and can move around by holding to something. The improvement seemed to stop in about June or July of 1946, and the patient has remained in about the same condition since then. In January 1947, when I examined her, the *Outstanding Physical Findings* were: pale optic discs, Babinski signs positive bilaterally, Oppenheim signs positive bilaterally, hyperactive reflexes in lower extremities, no abdominal reflexes, questionable involvement of the right facial nerve, ankle clonus sustained on right, Achilles clonus present on right, ankle clonus unsustained on left, but present. Mental status: Patient was entirely cooperative in attitude and made a satisfactory adjustment to the hospital's routine. There was nothing unusual noted in the stream of mental activity. Patient denied any feelings of depression or anxiety regarding her physical condition and did not express any particular concern. Objectively, mood appeared to be strikingly complacent toward her obviously serious neurological condition. There were no special preoccupational trends and no delusional ideas. Patient was very casual in relating in a chronological fashion the course of her illness since 1945. Sensorium was intact. Patient was fully aware of her physical handicaps and seemed to assume that her condition might rapidly improve. Medication given: B_1 and B complex daily, liver —one cc.I.M. twice weekly, histamine 0.275 mg., in 250 cc. saline each day, begun on January 14, 1947 and given for thirty-one consecutive days; prostigmine bromide, one tablet three times a day; 1/150 grain of atropine sulfate daily orally. At the time of discharge, the patient was very much improved and was able to walk and insisted that her vision was improved. At the time of her discharge, however, it was considered that her improvement might not be permanent. Although the patient has not been seen since her discharge, she reports regularly by mail, writing the letters herself, and obviously has a slight tremor; although comparison of her letters indicates that the tremor is lessening. In July of this year she wrote that she was feeling much weaker and suggested that she might need another course of histamine. However, in her last report to us, September 1948, she stated that she had received a letter from the National Multiple Sclerosis Society which sent her a membership card; she said that she continued to improve and that she wanted to come to visit us to show us how well she can walk across the room without her cane. She continues to take prostigmine bromide.

Case 4:

Miss V.R.B. White female, AGE 25. (Very brief summary of admission note made April 1947). Patient was seen April 11, 1947, eight days prior to admission to hospital. The history developed that in 1942 patient was troubled with double vision with sudden loss of vision in her left eye and partial impairment in right eye. This condition improved and she seemed to get along well until 1946 when the left leg began to drag. She had been treated chiefly with vitamins from 1942 to 1946. Her condition improved again until four weeks prior to admission to hospital (BHS) when her left arm became numb. A week after this her right leg grew numb. She began to stagger as though she were intoxicated. Her foot hit the ground. Her left arm was not paralyzed, but it felt "useless." Patient described her legs as feeling heavy; she felt as though she were going to fall. There was a sensation as though there were a belt around her hips. Her vision was considerably improved over that of 1942. She could distinguish objects; she stated that she was 40 per cent color blind. *Mental Status:* Patient was unusually cheerful and even euphoric. *Neurological Findings:* Marked pupillary irregularity—pale optic cups, positive bilateral Babinski, hyperactive reflexes in lower extremities, diminution of abdominal reflexes. *Treatment:* Patient received thirty-day course of histamine acid phosphate, prostigmine bromide 15 mg. three times a day, and atropine sulfate gr. 1/150th daily. Patient was discharged from the hospital very much improved and the improvement has remained sustained. She continues to take the prostigmine bromide and the atropine.

Case 5:

Mr. J.E.H. White male, AGE 50. Admitted to hospital in December 1947. History developed that patient had been ill for nearly two years. He complained of a severe headache which began at the top of his head and went "all the way down his spine." He complained of dizziness and lost his balance when he shut his eyes. An exploratory craniotomy had been performed in May 1947 by a neurosurgeon who suspected a cerebellar tumor; but no tumor was found. Patient did not complain of headache after the operation, but was referred to us in December 1947 because of a personality change. Mental symptoms were manifested particularly by irritability, depression, suicidal tendencies, and a mild paranoia. Patient complained of a "funny feeling" in the back of his head, and some weakness of his eyes. *Outstanding Objective Neurological Findings* revealed normal fundi, no extraocular palsy but a definite horizontal (bilateral) nystagmus; other signs referable to cerebellar involvement, particularly cerebellar ataxia, requiring a cane and other support to walk; hyperactive reflexes in lower extremities; marked

degree of cerebellar ataxia. A cerebellar type of Multiple Sclerosis was diagnosed. Patient was given prostigmine 15 mg. three times a day, and nicotinic acid 50 mg. three times a day, along with 1/150th gr. of atropine sulfate twice a day, or as needed for cramps produced by the prostigmine. Histamine regimen was started, but the patient remained in the hospital only a week, necessitating the termination of the histamine. A report received on March 16, 1948 stated that the patient was not getting along so well.

Case 6:

Miss L.F.M. White female, AGE 50. Patient admitted herself to hospital on March 25, 1947. She complained of weakness in her right arm, difficulty in walking, sensation of coldness in right leg below the knee. She stated that her symptoms first began seven years ago with weakness in the right arm and right leg, and she has been slowly getting worse; although there have been periods of time when she thought she was somewhat better. Her mental status as noticed by her friends: Patient was definitely euphoric, always in good spirits, and quite talkative. The examinee made the following statement: "With reference to insight, patient is well aware of her physical incapacities and is accepting gradual increase of symptoms in the philosophical way that most patients of this type do." *Neurological Findings:* No nystagmus was noted and the fundi were normal; no extra-ocular palsies; there was a bilateral Hoffmann, a bilateral Babinski, and an absence of abdominal reflexes; hyperreflexia on the left, sluggishness on the right (because of a right-sided spastic contracture, patient was unable to walk or stand). *Treatment:* Histamine acid phosphate regimen extending over a period of thirty days; as well as atropine sulfate and prostigmine bromide. There was practically no improvement and the follow-up since her discharge shows that her condition has remained about the same.

Case 7:

Mrs. E.A.W., White female, AGE 40. Examined August 16, 1948. This patient was sent in chiefly because of a depression, bad eyesight, and difficulty in walking. The history developed that in January of 1948, following a hysterectomy, she suddenly had a disturbance of vision and was not relieved by glasses; for a period of about four days, her right hand and arm "had no feeling"; she was seen at that time by a physician who did not think that there was anything organically wrong. She continued to work and "shop around" seeing different doctors, and was finally referred to me in August of 1948, when it was obvious that she was suffering with Multiple Sclerosis. The outstanding neurological findings were a slight bilateral temporal pallor, diplopia when looking to the left, bilateral nystagmus with quick component to the left, dysmetria, and an intention tremor in the right upper extremity; hyperesthesia of the right lower extremity, bilateral Babinski, deep reflexes in the lower extremities slightly exaggerated, abdominal reflexes absent, slight spasticity in the right lower extremity. Serology negative; spinal fluid shows a slight increase in proteins.

Case 8:

Mrs. C.F.D. White female, AGE 21. Patient was seen May 6, 1948. One month before consulting me, patient suddenly lost sight completely in her left eye and vision in the right eye was blurred; also there was numbness in the left side of her face and tongue; her mouth drew to the left and she was unable to close her right eye. The *outstanding Neurological Findings* revealed a marked blurring of vision to the right and left with a definite scotoma on the right. Pupils were irregular—the right larger than the left and both reacted very sluggishly; there was a right peripheral facial nerve palsy; there was no nystagmus noted; all reflexes were sluggish and required reinforcement; the abdominal reflexes were absent. *Treatment:* Patient was given a course of histamine extending over a period of thirty days, following which time she stated that she felt very much improved; her vision was especially better on the right; whereas, the vision on the left was about the same. However, she thought she could see a little better to the side. She complained of numbness and tingling in her legs and especially in the right. Visit in *July 1948:* There was a suspicion of a beginning nystagmus; however, the facial weakness had disappeared entirely; there was a little weakness of the left hand-clasp and some weakness of the toes of the right foot. She also stated that she was having a little trouble with bladder weakness. *Treatment:* Following the course of histamine in May, she was placed on B-complex and prostigmine bromide. Another course of histamine was advised in July; however, she decided to wait. She talked about going to a chiropractor. Incidentally at the time of her last visit, she stated that she remembered that some two years before, she had some numbness in her right leg which lasted for a couple of weeks and the doctor said it was neuritis.

Case 9:

Mrs. E.J.W. White female, AGE 27. Patient was first seen June 19, 1948. She complained of a dead feeling in both feet. A week before appearance of neurological symptoms, she developed considerable temperature, following which time she became very unsteady; and was practically unable to walk at the time she was examined. Patient stated that in December of 1947, six months after her child was born, she noticed first that she lost the feeling in the balls of her feet and toes. She could not tell, except by wiggling her toes, that she had her stockings on; a short time later she noticed urinary urge—about eight times a day—but had difficulty starting and later had difficulty voiding, and

—Concluded on page 137

Case Report of Laceration of the Liver

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and
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The purpose of this discussion is to illustrate a rather unusual injury: that is, acute trauma to the liver with resultant laceration, and the associated syndrome and complications.

Severe and extensive lacerations of the liver in the apparently well adult are rather uncommon among the sequelae of trauma. Although a solid viscus is more frequently injured than the hollow viscera, the incidence of lacerated liver is thought to occur approximately once in every 2,000 acute traumatic abdominal cases. The right lobe is more frequently subjected to laceration than the left, which is explained by its location beneath the thoracic cage and its relatively greater size. The injury is usually acquired by blunt force to the abdomen such as being struck by a blunt object, or a crushing or squeezing type of injury or torsion. The liver may exhibit several types of lacerations. Probably the incidence of small subcapsular lacerations or central ones is much higher than is generally suspected and their manifestations are so minimal or marked by other injuries that the diagnosis is seldom made or at least substantiated. On the other hand, multiple lacerations or transection of a lobe are rarely seen at operation but rather at necropsy because of the immediate massive hemorrhage. Less severe lacerations may show a typical picture of a chemical peritonitis with evidence of internal hemorrhage and shock. The patient may appear to improve only to relapse because of an exacerbation of the bleeding. Consequently the authors feel that this case report may be of interest to the general surgeon who is faced with the problem of diagnosis and management of acute trauma to the abdomen and its visceral contents.

Case Report H.E. No. 375190 1948

The patient was admitted to the hospital following an automobile accident at which time he was believed to have struck his head and his lower chest. He complained of some headache, weakness and epigastric pain. The past history consisted of only an appendectomy in 1931 and generalized arthritis for which he has been under treatment. The essential findings on physical examination were slight irregularity in the size of the pupils with the right one slightly dilated; a superficial laceration through the right eyebrow. The patient's skin was cold and moist with an odor of alcohol from his breath. The chest was clear. The heart revealed only a tachycardia of 110. The Blood Pressure was 60/0; respirations 36. There was point tenderness in the epigastrium without rebound and minimal upper abdominal spasm. Peristalsis was absent. The temperature was 96° on admission. R.B.C. 4.1 million and Hgb. 75%. W.B.C. 9600. Shock therapy was instituted but the B.P. failed to respond to blood and plasma. The patient was placed in oxygen but the respirations elevated to 45. Eight hours after admission a repeat R.B.C. was 2.8 million, Hgb. 65%, F.B.S. 154 mg. and the urine revealed a high trace of albumin and a 2+ sugar reduction. The hematocrit was 36.

Despite the obvious internal bleeding from a rupture of a solid viscus his general condition did not permit surgery.

After 48 hours his B.P. was 96/60, respirations down to 40, temperature 99.2 and he complained of epigastric pain penetrating to the back and pain in the region of his left scapula. The Hgb. was 68% and the R.B.C. 3.6 million. The urine at this time exhibited a high trace of albumin

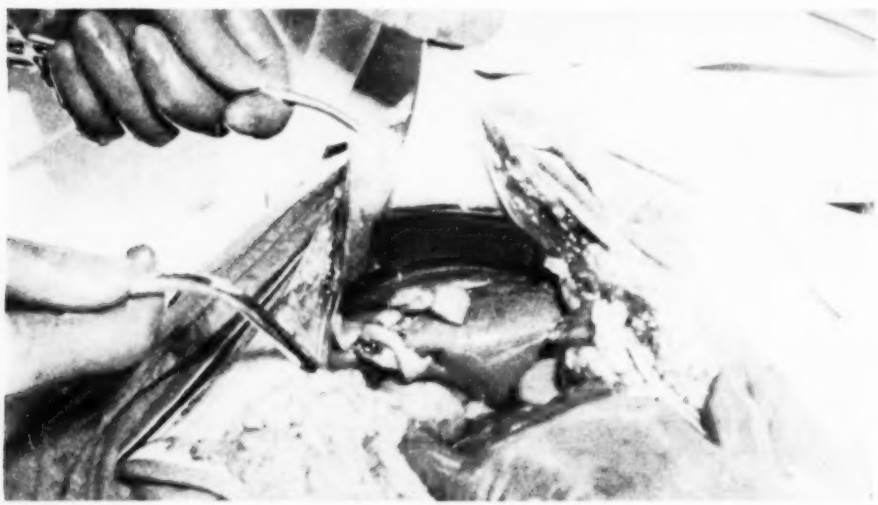
and 2+ sugar reduction. F.B.S. 180 mg. The N.P.N. was 31.

Surgery was elected at this time and under general anesthesia exploratory laparotomy was done which revealed a large volume of free blood within the abdomen and a laceration through the right lobe of the liver medial to the gallbladder bed. This was repaired with #2 chr. sutures inserted through Gelfoam and in addition Gelfoam was packed along the margins of the laceration. With complete hemostasis the abdomen was closed without drainage.

Postoperatively the patient had an elevation of temperature for only two days; the urine continued to show both sugar and albumin for five days before clearing up. The N.P.N. rose as high as 60 before returning to normal. The urinary output was only 200-500 cc. daily for four days and the B.P. fluctuated from 240/140 to 180/100 for five days after which time it stabilized at 130/80. On the second P.O. day he had clinical jaundice with an icteric index of 45. The Van den Bergh was immediate direct, cephalin flocculation 3+, thymol turbidity 1+, urobilinogen negative, urinary bile positive, total protein 4.7, A/G 2.0/2.7. On the fifth P.O. day the patient had spontaneous diuresis at which time the B.P. began to fall. The jaundice gradually faded and on the twelfth hospital day the patient was clinically well and all laboratory values had returned to within normal limits and the patient was discharged from the hospital for convalescent care.

Discussion

Several points in this rather unusual case are worthy of rather detailed discussion and speculation as to the physiological mechanisms involved. To approach these in a logical fashion it would seem they may best be taken in the order in which they occurred. First, the acute trauma to the liver with the resultant laceration and hemorrhage may well account for the sustained shock. However, the presence of persistent glucosuria and hyperglycemia might best be explained on the basis of acute liver malfunction as a result of the trauma. This is further substantiated by the postoperative jaundice and laboratory evidence of liver damage. That jaundice may occur from the absorp-



The lacerated livers with Gelufoam packs sutured in place. The one on the under surface of the liver is not better visualized because here it was that the liver was almost completely divided. The one on the superior surface of the liver can be readily seen.

tion of blood from the peritoneal cavity is a well known fact. However, the laboratory studies do not support this possibility. The liver failure in this particular instance, as evidenced by the early disturbance of the function of glycogenesis and later jaundice, the presence of bile in the urine, 3+ cephalin flocculation, reduced total protein and shift of the A/G ratio, all support the possibility of an acute traumatic hepatitis or a manifestation of the hepatorenal syndrome. However, the changes within the liver were reversible from the clinical and laboratory standpointt, although later sequelae cannot be predicted at this time.

The third and probably most interesting complication was the development of a lower nephron nephrosis. The patient experienced a period of some 48 hours of sustained shock prior to operation and then was subjected to a surgical procedure under general anesthesia. These several factors are generally accepted as etiological agents in the development of lower nephron nephrosis. The postoperative hypertension with oliguria and albuminuria and minimal edema are the typical features of this form of renal pathology. In turn, the spontaneous diuresis with rapid subsidence of clinical manifestations gives supportive evidence toward the postulation of a lower nephron nephrosis. This syndrome may be considered as an entity in itself, or probably a more logical conclusion could be drawn that the entire picture is one of a hepatorenal syndrome which resulted from acute injury to the liver with concomitant severe blood loss.

Summary and Conclusions:

The case presented was one of extensive laceration of the right lobe of the liver secondary to trauma to the lower chest without rib fractures.

The patient exhibited early liver disorder in the function of glycogenesis.

Later postoperative manifestations of liver malfunction and the evidence of lower nephron nephrosis.

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499 PLEASANT STREET

GENERAL PRACTICE

Hospital Obstetrics by General Practitioners

To the Editor:

Thank you for your letter of January 20. I was most flattered to find that MEDICAL TIMES saw fit to print a condensation of my recent article in *Surgery, Gynecology and Obstetrics.*

Your condensation brings out all of the points which I had wanted to make in the original article, chief among which was to point out that general practitioners, working in small general hospitals, can and do do good obstetrics.

Since the article was published, I made another statistical survey of the same two hospitals for the past year, finding that the same results are being had. In fact, the infant mortality for the year is better. And I know that a greater percentage

—Concluded on page 148

EDITORIALS

"Wassermann Test" For the Legislative Proponents of Bureaucratic Medicine

There is no reason to suppose that the astronomical funds built up by a compulsory sickness insurance wage tax would not be diverted from an alleged "reserve" for other purposes, just as has happened in the case of the Social Security set-up.

If all legislative bills could be barred that did not carry downright provisions against such indirect use of tax funds, the promoters of political medicine would liquidate themselves; the whole sorry movement would then die of simple inanition.

The position of a politician on this matter would determine his sincerity regarding the public welfare.

All our country needs is improvement and expansion of our public health services nationally and grants-in-aid *to the states* for the *voluntary insurance of the indigent*. "The public health services benefit all of the people and not just the employed population"—a wise remark recently made by Mrs. Elinore Morehouse Herrick, noted labor relations expert and member of the editorial staff of the *New York Herald Tribune*.

Subversive Listings

The criticism of many religious and educational institutions and organizations on suspicion of subversive philosophy or practice has compelled even such bodies as the Y.W.C.A. to insist in the press and otherwise upon their loyalties and integrity (*New York Times*, January 28, 1949).

As the tension and struggle grow keener between the proponents and adversaries of political medicine we should not be surprised to find the latter characterized by some official spokesman as working against the Government of our country.

What an ironical turn of events will transpire when we find the American Medical Association, the National Association of Physicians, and the medical press protesting that they are not subversive.

The Relations of Socialized Medicine and Euthanasia

A. C. Ivy, expert medical advisor to the prosecution at the Nürnberg Medical Trial, points out [*J.A.M.A.* 139:131 (January 15) 1949] that the compulsory sickness insurance system of medical care in Germany, "after operating over a period of years, led to a debased regard for the poor and underprivileged patients. Patients were too frequently treated as numbers rather than individual human beings with inalienable rights and dignity."

Ivy also points out *(ibid.)* that the ideology of the *Herrenvolk* also led to a debased regard for the poor and underprivileged.

The same authority accounts for the euthanasia of the aged, the chronically ill, "useless eaters" and the politically undesirable by the joining of the two factors cited.

Among the risks of setting up a compulsory sickness insurance system in this country would be a division of classes that would facilitate and accredit the practice of euthanasia.

The Antistiffness Factor and Arthritis

Is it possible that the lack of the antistiffness factor studied by von Wagtendork and Wulzen at the Oregon State College several years ago may play some

part in the etiology of certain forms of arthritis, and is it probable that some form of dietary supply will be developed whereby prevention, palliation or cure will become available?

The purified factor in question has been obtained in very small amounts at the Oregon School of Science but it deteriorates rapidly; it seems that the assay method is of no use in gauging the antistiffness potency of various products.

Joint alteration with stiffness can be developed in guinea pigs fed certain diets and this has been remedied by feeding crude products—cream and molasses. Blackstrap molasses, the form employed for this purpose, is the exhausted residue from the syrup from which all recoverable sugar has been extracted; it is said to carry an appreciable quantity of the factor; this material is used in the preparation of cattle feeds and in the manufacture of ethyl alcohol.

But confusion has arisen by reason of the failure of S. E. Smith of the New York State College of Agriculture at Cornell University to cure induced stiffness in experimental animals with sugar cane juice supplied by Professor A. G. Keller of the Louisiana State University. Professor Smith is even unconvinced that the antistiffness factor has really been isolated.

No striking clinical evidence as to the use of the antistiffness factor in arthritis has come to our attention, which seems odd, since, as we have pointed out, at least two factor-bearing substances are known.

Perhaps apropos was the work of Professor Frazer at the Toronto General Hospital and of Dr. Albert G. Bower of Pasadena [MEDICAL TIMES 76:229 (June) 1948] in influencing the course of arthritis favorably when malnutrition and colonic visceroptosis were factors. Their diets consisted of maintenance protein, relatively low carbohydrate and high fat, plus wheat germ and brewer's yeast, and milk or milk products, which seem to imply more or less cream. The aim was to make the patients gain weight rapidly, correct the visceroptosis, and limit the production of bacterial allergens. But they may have been unwittingly supplying the lacking factor, in part.

Further inquiry from this antistiffness angle would seem to be in order.

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MULTIPLE SCLEROSIS

—*Concludede from page 132*

her bladder would fill up, causing great pain. She consulted medical advisers and was told that she had lost muscular control of the bladder; as a matter of fact, one physician told her she needed an operation. She developed a bladder infection and was given 200,000 U. of penicillin. *Outstanding Neurological Findings:* Tingling in lower extremities; absence of abdominal reflexes; bilateral Babinski; hippusthesia, scattered, below the unbilicus as well as a diminution in position and vibratory sense. Rhomberg positive; spinal fluid essentially negative. *More History:* Later it was developed that in 1944 she recalled having some difficulty with her legs, which she described as a difficulty in maintaining her balance, as well as vague disturbance in feeling. Since then she had other episodes which she described as insecurity of balance; she had difficulty in going upstairs at night; she has always had difficulty walking on her heels; there were also periods when she felt that she was a little awkward with the use of her hands and experienced "dead feelings" in the palms and fingers. Once in 1945 she had difficulty in holding a pen. She insisted, however, that most of her very disturbing symptoms dated from December of 1947. *Treatment:* She was given a thirty-day course of histamine treatment and was very much improved; she is now under observation and is receiving prostigmine bromide. The most striking improvement is that her bladder control has improved.

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CONTEMPORARY PROGRESS

MEDICINE

Dicumarol Therapy in Congestive Heart Failure

J. H. Wishart and C. B. Chapman (*New England Journal of Medicine*, 239:701, Nov. 4, 1948) report the use of dicumarol in the treatment of 61 cases of congestive heart failure. This treatment was employed to decrease the incidence of embolic phenomena. All the patients in this series had definite symptoms of congestive heart failure; patients with dyspnea and basal rales as the only sign of decompensation were not included. Before dicumarol therapy was begun, a careful study of the patient was made to determine if there were any contraindications to the use of the drug. If no contraindication was present, blood was withdrawn for determination of the prothrombin time, and the initial dose of dicumarol, which was usually 200 mg., was given. In some cases small doses of heparin were given intramuscularly in addition to the dicumarol for the first twenty-four to forty-eight hours. After dicumarol therapy was begun determinations of prothrombin time were made daily and the dosage adjusted so that prothrombin concentration was below 30 per cent but above 10 per cent. There were 20 deaths in the series, a mortality of 32.8 per cent; none of the deaths could be definitely attributed to "classic pulmonary embolism," and in only one case was there any possibility that death could have been due to pulmonary embolism. Autopsy was done in 12 cases and infarcts other than myocardial were found in 6 cases; but in 5 of these cases it could be determined that the infarcts developed before dicumarol therapy was begun or after it was discontinued. On the basis of clinical findings definite pulmonary infarcts developed in 2 patients and renal infarct in one case during adequate dicumarol therapy. On the basis of the clinical and autopsy findings, therefore, embolic phenomena developed in 4 cases, or 6.5 per cent of the 61 cases, during adequate dicumarol therapy. On the basis of previously published reports, the development of embolic phenomena was to be expected in 22 per cent of a comparable group of cardiac patients without dicumarol therapy. On the basis of these results the authors conclude that dicumarol apparently gives protection to the cardiac patient from thrombosis and embolism, when most needed, i.e., in the period of congestive failure.

COMMENT

This shows a definite reduction in the frequency of embolic phenomena when dicumarol is used. ***W.W.T.***

The Clinical Use of Radioactive Iodine

S. C. Werner and associates (*Bulletin of The New York Academy of Medicine*, 24:549, Sept. 1948) report the use of radioactive iodine of eight-day half life (I^{131}) as a tracer in diagnosis of thyroid disease and in the treatment of 40 cases of toxic goiter. The use of I^{131} as a tracer was found to be of diagnostic value if stable iodine or antithyroid drugs had not been given shortly before the study was made. With a tracer dose of 50 to 75 mc., the normal uptake by the thyroid is 20 to 30 per cent; an uptake of over 40 per cent indicates definite hyperthyroidism, an up-

take of less than 10 per cent, hypothyroidism. In the treatment of the 40 cases of toxic goier, from 3 to 4 mc. of I^{131} were given; 13 of the patients showed no response; 7 were treated again and 4 failed to respond. Of the 34 patients treated once, or if necessary twice, and followed up for four months or more, 30 have been put in remission. The other 6 patients, who failed to respond to the first treatment, have been re-treated too recently to be included in this report. An estimate of the size of the thyroid gland, although not accurate, was made to permit calculation of radiation dosage. In 15 cases in which the dosage was 100 or more mc. per gram, only 2 failed to show satisfactory remission. With lower dosages, only about 50 per cent showed satisfactory results. Calculating the dosage on the basis of equivalent roentgens, it was found that results were good in all but 2 of 13 treatments with 6000 e. r. or more; with a dosage of 3,000 to 6,000 e. r. 50 per cent good results were obtained. There were 4 cases of transient hypothyroidism, all but one of which followed doses above 6,000 e. r. In addition to these 4 cases of transient hyperthyroidism, there were 7 cases in which sensations of a head cold or sore throat, or a cough, developed several weeks after treatment; 2 cases with marked tenderness of the thyroid; and 3 cases of a "flare-up" of toxicity in the month after treatment. There was no radiation sickness and no evidence of any radiation damage.

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COMMENT

Evidently of help in diagnosis and treatment. *M.W.T.*

One Hundred Cases of Miliary Meningeal Tuberculosis Treated with Streptomycin

P. A. Bunn (*American Journal of the Medical Sciences*, 216:286, Sept. 1948) reports 100 cases of acute miliary tuberculosis and/or meningitis treated with streptomycin in 47 Veterans Administration Hospitals. Of 22 patients with miliary tuberculosis without meningitis, 16 or 73 per cent survived. Of the patients with tuberculous meningitis, 37 per cent survived, the highest survival rate being in the group with meningitis alone, without miliary tuberculosis (16 survivals in 43 cases). There were 40 survivors in the entire series of 100 cases at the time that this report was submitted. Eight months later, 24 of these 40 patients were known to be living; 15 had died, and one was lost to follow-up. Three of these deaths occurred in patients treated originally for miliary tuberculosis; all of these patients subsequently developed meningitis; 7 deaths occurred in those originally treated for meningitis; in 5 death was due to relapse or progression of the original disease, and in 3 to progressive pulmonary disease (without evidence of meningeal disease). There were 5

deaths in the group with combined miliary and meningeal disease, all due to meningitis, 3 showing no pulmonary miliary tuberculosis at autopsy. Of the 24 patients surviving, 8 have active foci of tuberculosis other than the disseminated form; 1 is undergoing a fourth course of treatment for meningeal relapse, after "cure" of the miliary lesions for which he was first treated. There are 15 patients who are either free from tuberculosis or show arrested lesions; only one of these patients was treated originally for combined miliary and meningeal tuberculosis, 7 were treated originally for miliary tuberculosis and 7 for meningeal tuberculosis. Various dosages of streptomycin were used in this series of cases; a daily dosage of 1.8 gm. by intramuscular injection and daily intrathecal injection of 0.1 gm. in cases of meningeal disease were suggested, but this schedule was not used in all cases. Of the 24 surviving patients, 10 have moderate to severe impairment of labyrinthine function, one is deaf, and 3 have neurologic sequelae.

COMMENT

Encouraging. ***M.W.T.***

A New Treatment for the Relief of Obliterative Diseases of Peripheral Arteries

I. Mufson *(Annals of Internal Medicine,* 29:903, Nov. 1948) reports the use of an intra-arterial infusion of histamine in the treatment of endarteritis obliterans due to thromboangiitis or arteriosclerosis and causing severe insufficiency of the peripheral arterial circulation. The injection is given into the femoral artery; the pressure at which the solution is introduced is regulated so that it is higher than the diastolic pressure in the artery. The solution employed contains between 1.39 and 2.75 mg. of histamine acid phosphate (equivalent to 0.5 to 1.0 mg. of histamine base) in 500 cc. normal saline. Infusions are given weekly at first or in cases with severe symptoms, biweekly. Over 500 injections have been given without any local intra- or extra-arterial complications. The walking tolerance of each patient is determined as the number of blocks he is able to walk without being forced to stop by pain in the leg. The "sleep tolerance" is determined as the number of hours the patient can be in bed in a horizontal position before being awakened by pain in the calf of the leg. When the talking tolerance was increased to 10 blocks, treatments were given only once a month; if walking tolerance was increased to 18 to 20 blocks, treatment was discontinued, but could be resumed, if there was any loss of walking tolerance. This response to treatment occurred in 51 per cent of the patients. In 33 per cent, walking tolerance increased to 6 to 10 blocks, when the interval between treatments was lengthened without a relapse but with no further improvement. In 16 per cent, there was no or negligible improvement in walking tolerance after six treatments. Sleep tolerance was increased in all cases, with much relief to the patients. Improvement in both walking and sleep tolerance occurred after three to six injections. After each intra-arterial injection there is improvement in the color of the skin, an increase in skin temperature, and increased diffusion rate of radioactive sodium; the degree and the extent of these reactions depend on the extent of the arterial block and the available collateral circulation. These responses to a single intra-arterial injection are not necessarily closely correlated with the clinical response to therapy; but when these responses are correlated with all variable factors including extravascular causes of spasm, it is possible to grade the extent of the occlusion and to prognosticate "with some degree of accuracy" the outcome of the histamine therapy.

COMMENT

Further experiments with this treatment will be awaited with interest. ***M.W.T.***

NEUROLOGY

Methyl Hydantoin (Mesantoin) in the Treatment of Epilepsy

N. A. David and associate *(Journal of Nervous and Mental Diseases,* 108:118, Aug. 1948) report the use of a new anticonvulsant drug, 3-methyl, 5-5 phenylethylhydantoin (mesantoin or methyl hydan-

toin) in the treatment of 20 patients with epilepsy, 11 of whom had grand mal seizures, and one jacksonian epilepsy. This drug proved more effective in controlling grand mal seizures than any drug previously used in 7 of the 11 patients with this type of epilepsy. In the cases of petit mal, the number of attacks was definitely reduced. In the cases with both grand mal and petit mal attacks and in the case of jacksonian epilepsy, the results were not conclusive, as the period of observation was too short. The toxic symptoms observed were dermatitis in 3 patients, gastritis in one, and an episode of toxic psychosis in one (after only 4 tablets had been given). None of the patients showed "dopiness," hyperplasia of the gums, or depression of the white cell count. On the basis of their findings the authors conclude that methyl hydantoin is an effective drug in grand mal epilepsy, and is especially indicated in cases of this type in which phenobarbital causes undue mental depression or in which either phenobarbital or diphenylhydantoin sodium is not effective. It is of more value in petit mal than diphenylhydantoin sodium and should be tried in cases of this type in which other drugs are not effective or not well tolerated.

COMMENT

To this reviewer the occurrence of toxic symptoms in 5 of 20 cases (25 per cent), while a small series, indicates the degree of care required when this drug is used. Certainly this degree of toxicity is not manifested when diphenylhydantoin sodium is used.

However, in cases where neither luminal nor sodium diphenyl hyantoin is effective, nor can be tolerated, the possibility of another effective anti-convulsant drug is welcomed. *H.R.M.*

Pneumoencephalography in the Diagnosis of Cerebellar Atrophies

L. Uzman (*American Journal of Roentgenology*, 60:293, Sept. 1948) reports 5 cases in which the diagnosis of cerebellar atrophy was confirmed by pneumoencephalography. All the patients were men, in whom symptoms had developed after the third decade of life; there was no family history of similar neurological disease in any case. The chief complaint in these cases was difficulty in walking; reeling and staggering occurred in the more severe cases; all the patients walked with a broad base. Cerebellar asynergia, dysmetria and tremor were present in the lower extremities, but only to minimum degree in the upper extremities. The encephalographic studies in these cases showed an increase in the size of the basal posterior fossa cisterns, indicating a reduction in the size of the cerebellum. The 5 patients were admitted to the Neurological Service of the Boston City Hospital within a period of nine months; in such cases the use of encephalographic examination as a routine procedure appears to be "almost a necessity." Not only does it confirm the clinical diagnosis by a relatively simple procedure, but in larger series of cases, the clinical symptoms might be correlated with the anatomical changes as shown in the encephalograms during the evolution of the disease.

COMMENT

Undoubtedly the examiners were supremely confident of the fundamental nature of the disease process in these cases, for ordinarily there is considerable reluctance to introduce air by the lumbar route in patients with physical signs pointing to the posterior fossa. The courage of the investigators was rewarded when they obtained "a diagnostic clincher" in the x-ray findings. *H.R.M.*

Modification by Curare of Circulatory Changes During Electrically Induced Convulsions in Man

M. D. Altschule and K. J. Tillotson (*Archives of Neurology and Psychiatry*, 59:496, April 1948) report a study of the effect of curare on the circulatory changes that occur during electroshock therapy. Curare is widely used to decrease the severity of the seizures in electroshock therapy. The circulatory changes that have been observed during electroshock therapy are a rise in venous pressure, acceleration of circulation time, a rise, followed by a fall, in arterial pressure, and changes in cardiac rhythm characteristic of vagal hyperactivity. In the present study, the effect of curare in 88 electroshock treatments in 20 patients was studied; "intocostrin"

was used in 27 treatments and *d*-tubocurarine in 61 treatments. Curare does not abolish the convulsion in electroshock therapy; the muscular contractions are less violet, but the seizure is often somewhat prolonged. The chief effect of curare on the circulatory changes characteristic of the electroshock is the reduction of the degree of the rise in venous pressure; while there was some rise in venous pressure in each experiment, it was definitely less than in uncurarized patients. The electrocardiographic changes were of the same type, but were usually less prominent with curare, except that in these experiments there was an increase in the incidence of ventricular premature beats after seizures in curarized patients; most of the patients were "well advanced in years," so that it is difficult to evaluate this finding. In all cases *d*-tubocurarine was as effective as "intocostrin" and caused no untoward reaction.

COMMENT

Since the use of electroshock therapy is widespread, and in selected cases its use is beneficial, such studies as this one are to be commended. It is noteworthy that this study revealed no findings against the use of the procedure. ***H.R.M.***

GYNECOLOGY

Smear Diagnosis of in Situ Carcinoma of the Cervix

F. W. Foote and Katherine Li (*American Journal of Obstetrics and Gynecology*, 56:335, Aug. 1948) report a study of smear diagnosis in 18 cases of intra-epithelial epidermoid carcinoma, or carcinoma in situ, of the cervix. In all cases smears were taken from the cervix as well as from the vaginal vault. Of the 18 patients in this series, 12 showed no gynecologic symptoms; one complained only of somewhat excessive yellowish discharge; and 5 had vaginal bleeding which was not excessive or continuous, and had usually been present for only a short period. On vaginal examination, the cervix was found to be "clean" or to show only slight erosions in some cases; in others there was more extensive erosion, chronic cervicitis, ulceration or laceration; in only 2 cases was a diagnosis of early carcinoma or possible carcinoma made by the examiner. Positive biopsies were obtained in all cases; and in 15 of the 18 cases the diagnosis of carcinoma in situ was confirmed by histological examination or hysterectomy or trachelectomy specimens. In 14 of the 18 cases, the initial smears taken from the cervix showed unequivocal cytological evidence of carcinoma, while such cytological evidence of carcinoma was obtained from the vaginal vault smears in only 9 cases. The vaginal smear was not positive in any case in which the cervical smear was negative. In the cases where both smears were positive, the number of cancer cells was much greater in the cervical smear, and hence the diagnosis more easily made from this smear. These findings suggest that cervical, as well as vaginal, smears should be used for the diagnosis of early carcinoma of the cervix. A positive smear report for uterine cancer, however, should never be considered an indication for major surgical or radiotherapeutic procedures without a positive biopsy or curettage.

COMMENT

Vaginal and cervical cytology in the detection of cancer of the cervix is the most important single diagnostic measure yet discovered in the cancer field. Formerly we have spoken of early diagnosis of cancer whereas as a matter of fact we were, by comparison, speaking of advanced cancer, because by the time the doctor made a positive diagnosis of malignancy of the cervix or corpus the lesion had already spread beyond the surface epithelium. How far was anybody's guess. Correctly enough the authors verified each cytological diagnosis by biopsy. This is a "must". No

woman should be subjected to the hazards (psychological and physical) of a positive diagnosis of cancer unless the physician is sure; and certainly no woman should have radical treatment for cancer unless she positively has a cancer. Therefore in order not to reduce this most wonderful diagnostic procedure to a common racket let us "move slowly but surely," keep this procedure honest, and thereby help to reduce the inevitable mortality of cancer of the cervix—as elsewhere in the body. *H.B.M.*

Preservation of Function in Cystic and Sclerotic Ovaries

Philip Jacobson *(Surgery, Gynecology and Obstetrics,* 87:31, July 1948) describes an operation for the preservation of cystic ovaries that he has used in 16 patients from whom both tubes and one ovary had been removed and the remaining ovary had become "inadequate." In these patients, the menstrual periods had become irregular and the flow diminished; there were menopausal symptoms, including increased emotional tension. Following operation the normal periodicity was restored and the symptoms relieved. The first step in this operation is exploration of the mesovarium with special reference to the number of blood vessels going to the ovaries and the presence of varicosities; if varicosities are present they must be taken care of first. When there has been a previous operation, as in the cases reported, the mesovarium is distorted by adhesions, rotation or malposition, and it must be restored to its normal relationship again so that the ovary is properly suspended. The method of separating the cortex from the underlying stroma of the ovary is described in detail. When this is done, cysts or corpora albicantia can be easily discovered by palpation with the finger, although they cannot be detected through the intact cortex. The corpora albicantia may be broken up with a pointed probe, but follicles should be enucleated, if possible. If follicles cannot be shelled out, they should be opened so as to inspect the interior and detect any smaller follicles within. The operator must consider the fact that the trabeculae of the stroma run parallel from the mesovarium to the free border and must work in that direction. In this way there is little bleeding or destruction of ovarian cells. The aim of the operation is to relieve obstruction and strangulation; to allow for possible expansion of the stroma, the cortex is not closed too tightly. The lower border of the open cortex is joined to the open peritoneum of the mesovarium, creating a new white line; only fine catgut is used. The ovary is replaced and sutured as nearly as possible to its normal position, well above the cul-de-sac. This method of exploring the ovary has been employed in other cases and may be employed in cases in which the diagnosis is not as clear before operation as in the 16 cases reported. It is a conservative measure that can be used in the treatment of nonproliferative cysts of the ovary, "the most common cause of ovarian failure."

COMMENT

Conservation of ovarian tissue can be a very important procedure. "The when and the how" has been discussed by the "big and little shots" for the past 50 years. In spite of this there are no hard and fast rules by which any surgeon may successfully conserve ovarian tissue. This is one outstanding example where individualization of a given case plus the judgment and tecanical skill of the operator is the only way to successfully preserve any degree of ovarian function. The author describes a procedure which we have found very efficacious. It preserves the circulation to the ovary, which is all important, better than any other procedure that I know about. Naturally the remaining ovarian tissue will function in direct proportion to the adequacy of its circulation, hence the surgeon who forgets this primary premise is doomed to failure. Because of a lack of understanding of the anatomy and pathology of the ovary, surgeons are still battling with their failures. To me, ovarian surgery is the most exacting type of operation with which the gynecologist has to deal. Likewise the most satisfying when successful. There is no happiness, unless it be that of the wedding day, that compares to the joy of a baby following resection of an only ovary—absolutely none. *H.B.M.*

A New Simple Physical Method for the Administration of Intrapelvic Heat

W. J. Reich and M. J. Nechtow *(American Journal of Obstetrics and Gynecology,* 56:590, Sept. 1948) describe a simple method for the administration of intrapelvic heat that can be used by the doctor

in his office or in the clinic or by the patient at home. "Thousands" of patients who need intrapelvic hydrotherapy are seen at the gynecologic clinic of the Cook County Hospital. The chief indications for this form of therapy are pelvic inflammatory diseases with resultant tubo-ovarian abscesses and parametrial or pelvic cellulitis. In some cases in which operation is indicated heat therapy is required postoperatively or preoperatively. For many years the Elliott machine has been used for intrapelvic heat therapy, but because of the large number of patients, appointments for such treatments have to be deferred. With the simple method recently devised an intravaginal latex bag is used through which warm water circulates. Treatment is given with the patient in the bathtub with a heavy Turkish towel on the floor of the tub. With the patient in the lithotomy position, the vaginal bag, lubricated with a little soap or lubricating jelly, is inserted into the vagina. The rubber tube of the bag is connected to the water faucet and the temperature and pressure are adjusted to the tolerance of the patient. Treatments are given daily, for twenty minutes at first, gradually increased to about one hour. When the treatment is completed and the water shut off, the bag is removed and dried; if the bag is used by the same patient each time, sterilization is not necessary, but the bag is cleaned by washing with weak soap solution. Intrapelvic heat therapy has proved of special value in younger women of the childbearing age in whom it often renders surgery for pelvic inflammatory disease unnecessary.

COMMENT

The intravaginal use of heat in the treatment of pelvic infections has been employed for about 25 years. The method of applying this heat is not well standardized. Almost every known method of applying localized therapeutic heat has been employed and with varying success. One very popular technic is the Elliott method. This is excellent but is not adaptable to "mass treatments." The apparatus is expensive, too bulky and mechanical, and is expensive to employ. The authors, therefore, have devised a very simple and inexpensive home method by which the patient can treat herself or the doctor or nurse can treat office or clinic patients. The apparatus consists of a latex rubber bag of appropriate size through which warm or hot water circulates. The patient lies in the bath tub in the lithotomy position, inserts the bag into the vagina, attaches the rubber tubing of the bag to the water faucet, adjusts the temperature and pressure of the water, and the job is begun. Treatments are given daily, beginning with a duration of 20 minutes and gradually increased to 1 hour. This is by far the easiest and simplest way to apply long continued heat to the pelvis. Try it. H.B.M.

Uterotubal Insufflation with Penicillin and Streptomycin Aerosols: A Preliminary Report

Monte Salvin (*Western Journal of Surgery, Obstetrics and Gynecology*, 56:-500, Sept. 1948) reports the use of aerosols containing penicillin and streptomycin for uterotubal insufflation in 62 cases. For this purpose a DeVilbiss nebulizer (No. 40) is attached to the usual insufflation apparatus just before it is connected to the cervical cannula. The solution for nebulization contains 500,000 units of penicillin and 500 mg. of streptomycin per cc. This combination of the two antibiotics renders it effective against both gram-positive and gram-negative organisms. Of the 62 patients in which the aerosol was employed for insufflation, 41 were found to have patent tubes and 21 non-patent tubes with pressures up to 200 mm. of mercury. None of these patients showed any untoward effect of the insufflation. Many of these patients had low grade pelvic infection with some tenderness over one or both tubes, a condition formerly considered a contraindication to tubal insufflation. But these patients showed no ill effect of the procedure, but rather a definite improvement after insufflation. This procedure, therefore, supplies an additional method for the administration of these antibotics in gynecological conditions in which they are indicated.

COMMENT

The thoughts and ideas of geniuses are never ending. They are apt to "pop out" in most unorthodox ways. The author's use of a mixture of penicillin and streptomycin aerosols by uterotubal insufflation is illustrative of what is meant. At first thought, his seems a

very queer way to administer the antibiotics yet on more mature thinking it seems like a very good method, although fairly complicated. We have had no experience with the method but can see no particular advantage in its use. We still believe that the "simplest way is the best way" and what is simpler than the conventional ways of giving any therapeutic agent—by mouth or by needle? Furthermore we do not agree with the author when he infers, though he does not directly say so, that the local effects on pelvic infection favor this method of giving these antibiotics. We think the weight of evidence is against any local effects except in open lacerated and/or contused wounds during, let us say, the acute infectious process. Antibiotics inhibit the multiplication of certain bactera but they do not necessarily kill these bacteria. They work best through the blood stream; not locally. H.B.M.

Amebic Vaginitis

B. B. Weinstein and J. C. Weed (*American Journal of Obstetrics and Gynecology*, 56:180, July 1948) report 4 cases of amebic vaginitis seen at the Touro Infirmary, New Orleans, within a period of nine months. No further cases of amebic vaginitis have been observed, although thorough examination for parasites have been made. In a review of the literature from 1916 to 1946, only 10 cases of amebic vaginitis were found. The chief symptom in the authors' 4 cases was a bloody vaginal discharge, without pruritus. Vaginal examination showed one or more granular lesions of the vagina and a similar lesion eccentrically placed on the cervix. In the cases reported in the literature, the findings were similar, except that a cervical lesion was not present in all cases. The trophozoite form of *E. histolytica* was demonstrated in the vaginal secretion; and this organism was also found in the stool in all but one of the authors' cases at the same time. In one case, the patient subsequently developed a sudden attack of diarrhea with *E. histolytica* in the stool, but there was no recurrence of the vaginitis. In all the authors' cases the vaginitis cleared up promptly when a course of Diodoquin and emetine was given combined with local treatment with cleansing douches and vaginal insufflation of Vioform powder, or, in one case, vaginal instillation of chinifon solution. As the incidence of amebic infestation in the United States is high, it is possible that cases of amebic vaginitis are overlooked or confused with other types of vaginitis.

COMMENT

Amebic vaginitis is a rare vaginal infection. It is well known that the incidence of amebic infestation in the United States is high, ranging up to 5 per cent. Therefore it seems fair to assume that either the physician "muffs" the diagnosis or the amebae do not gain access to or do not propagate in "routine vaginas". Only 10 cases were reported in the literature during the past 36 years (1916-1946). The authors report 4 cases seen by them during 9 months of 1946. The chief symptom is bloody or serosanguineous vaginal discharge with no pruritus. Speculum examination reveals a peculiar granular lesion of the vaginal mucous membrane and in 70 per cent of cases similar lesions appear on the cervix. We have never seen, or at least never diagnosed, a case of amebic vaginitis—no doubt we missed it. We agree with the authors when they say, "As the incidence of amebic infestation in the U. S. is high, it is possible that cases of amebic vaginitis are overlooked." Read this article carefully and thereby be prepared to make the diagnosis and give the proper treatment of amebic vaginitis—just in case you run across a case in your practice.

H.B.M.

OBSTETRICS

Vinbarbital Sodium for Obstetric Amnesia, Analgesia and Anesthesia

M. S. Lewis and J. B. Boddie, Jr. (*Southern Medical Journal*, 41:820, Sept. 1948) report the use of vinbarbital sodium for obstetric amnesia, analgesia and anesthesia in 3,000 cases. Vinbarbital sodium is the non-proprietary name of sodium 5—(1-Methyl-1-butenyl) barbiturate. In 2,444 cases all patients were given vinbarbital sodium by mouth with scopolamine and in addition vinbarbital sodium intravenously for the completion of labor. The initial dose of 9 grains of vinbarbital sodium with 1/150 grain scopolamine was given when the patient was in active labor with uterine contractions every four or five minutes;

1/200 grain of scopolamine was then given each hour as needed to maintain amnesia and analgesia; no more than three injections of scopolamine was given in any case, and the average patient received two injections. The average dose of vinbarbital sodium was 9 grains by mouth and 10 grains intravenously; the largest combined dosage was 18 grains by mouth and 20 grains intravenously in a prolonged labor (forty-six hours); the largest dose given intravenously was over 25 grains; this dosage did not cause depression or retardation of labor. Complete amnesia was obtained with oral vinbarbital sodium and scopolamine in 70 per cent of the patients in this group; after intravenous vinbarbital sodium, amnesia was complete in all cases. There were 1,144 spontaneous deliveries, and 1,307 operative deliveries; 61.4 per cent of the patients were primiparas, and 88 per cent of the operative deliveries were elective low forceps. There were 2,451 infants delivered (seven sets of twins), and 43 stillbirths and neonatal deaths; 13 died before the onset of labor, 10 died during labor; and 20 died after birth. Of the neonatal deaths, only 6 were fullterm infants, and 14 were premature, 9 of which were non-viable. Deducting the 13 deaths before onset of labor, the 9 non-viable infants, 2 neonatal deaths due to erythroblastosis fetalis, and 8 deaths due to definite obstetric complications, not related to the type of anesthesia, the corrected infant mortality is 0.4 per cent (11 deaths). In a group of 556 patients, vinbarbital sodium given intravenously was the only analgesia and anesthesia used. In this group, the patients were admitted in labor and given the initial dose as soon as possible after admission and approximately 95 per cent were delivered within two hours; the usual initial dose was 10 to 15 grains, the average total dose was 15 grains, the largest dose 25 grains. In 16 cases restlessness at the time of delivery was controlled by local anesthesia. Complete amnesia was obtained in 99 per cent of the entire group. Delivery was spontaneous in 331 patients, and operative in 229 patients; 66 per cent of this group were multiparas; and 78.4 per cent of the operative deliveries were elective or outlet forceps. There were 560 infants (four sets of twins) and 17 stillbirth and neonatal deaths; 10 died before the onset of labor; in the 7 neonatal deaths, only one was a full term infant and death was due to erythroblastosis fetalis; of the 6 premature infants 3 were non-viable; the corrected fetal mortality on this group is 0.05 per cent (3 deaths). In the entire series of 3,000 cases there was only one maternal death, not related in any way to vinbarbital sodium. Of the 2,978 infants born alive, 80.9 per cent breathed and cried spontaneously; 12.6 per cent were slightly asphyxiated, requiring only carbon dioxide and oxygen for resuscitation; 5.4 per cent were moderately asphyxiated and 0.9 per cent markedly asphyxiated, requiring other measures for resuscitation. No definite relationship could be demonstrated between the degree of asphyxiation and the total dosage of vinbarbital sodium or the time elapsing between administration of the drug and delivery.

H. R. Burkons (*American Journal of Obstetrics and Gynecology*, 56:549, Sept. 1948) reports the use of intravenous vinbarbital sodium for obstetric analgesia in 200 cases. In some cases this drug was used alone, the initial dose being 8 to 10 cc. In some cases vinbarbital sodium was given intravenously with scopolamine intramuscularly; in some cases previous medication had failed to induce analgesia and 5 cc. vinbarbital was given intravenously with good results. Of the 200 patients, 158, or 79 per cent, had complete amnesia; 38, or 19 per cent, had almost complete amnesia, with memory for isolated events, but complete relief of pain; only 4 patients had no relief. Drop ether or terminal spinal anesthesia was used for delivery. The pulse, respiration and blood pressure of the mother remained within normal limits after the administration of vinbarbital sodium. Approximately 77 per cent of the infants breathed spontaneously after delivery; in the remainder respiration was established "without any particular difficulty." The author considers that intravenous vinbarbital sodium is an effective method of obtaining rapid obstetric anal-

gesia, especially useful in multiparas in whom labor advances rapidly.

COMMENT

These two papers tell the usual story of the use of barbiturates for obstetric amnesia and analgesia. We all admit such agents are good in many ways and bad in a few, particularly for the baby. We do not yet have the ideal obstetric "pain killer" and yet we who do obstetrics must use what we think are the best and safest drugs. Our patients demand relief from the travail of labor and childbirth. The authors of these two papers have used vinbarbital sodium alone and in combination with scopolamine and/or demerol either intramuscularly or intravenously in a total of 3200 cases, which should give them the right to express an opinion. Their results were excellent; 98 per cent and 99 per cent respectively were charted as successful. This record is worthy of emulation. From over 25 years' experience, beginning with morphine and scopolamine (the old dammerschlof) back in 1917, we have employed about every type of obstetric "pain killer" and we can assure you these results are excellent for the mother. On the other hand, a "few" babies had to be resuscitated; but none were lost. This only further supports the fact that what is safe for the mother is not always as safe for the baby—which is why we do not have a perfect method of obstertic anesthesia and analgesia. Pick out a method and perfect your technic for its administration and you will be successful with it. "Practice makes perfect." H.B.M.

New Pregnancy Test: Use of Three Injections of Estrone in Oil

S. S. Garrett (*American Journal of Surgery*, 76:261, Sept. 1948) describes a test for pregnancy that he has employed in 250 patients with 100 per cent correct diagnoses, as shown by the follow-up. The test consists of three injections of estrone in oil (1 mg. each) given over a period of five days. If the patient fails to have vaginal bleeding within twenty-four hours after the last injection, she is considered to be pregnant. This test can be used on most women who desire to know if they are pregnant when their menstrual period is overdue. Subjects suitable for this test have a history of "reasonably" regular menstrual periods. The menstrual period must be definitely overdue, with no vaginal bleeding. The patient must be fairly healthy in appearance with no signs of severe anemia. Pelvic examination must show "reasonably" normal conditions, although possibly signs of pregnancy. The test must not be made if endocrine therapy has been given recently; thyroid medication is possibly an exception, as in 2 patients who were receiving desiccated thyroid by mouth as part of the treatment of sterility, pregnancy was correctly diagnosed by the test. In non-pregnant women who show vaginal bleeding within twenty-four hours after the last injection, the bleeding closely resembles the normal menstrual period; in a few cases the rate of flow was somewhat increased and the duration of the bleeding somewhat less than in the normal menstrual period; large clots or anything resembling tissue were not passed. The women who were pregnant reported no bleeding. This test is inexpensive and simple and can be performed in the doctor's office without the aid of an outside laboratory. The greatest shortcoming of this test is that it is not applicable to patients who show any vaginal bleeding. In the author's series in which the test was used, there were only 4 patients approaching the menopausal age; the test should be interpreted with caution in such women until data on a larger series of cases are available. When used in larger series, the test may not prove 100 per cent accurate, as in the author's series, but it should show a high percentage of accuracy.

COMMENT

There are many hormone tests for pregnancy, some reliable, some not so reliable; none are 100 per cent reliable. The test the author describes is simple but does not seem to this commentator to have a very sound physiological basis. The estrogens are given freely for all kinds of conditions—pregnant and nonpregnant—and I have not known that they regularly produce bleeding, even in much larger doses than are recommended here. It would seem to us that there are several pregnancy tests equally simple and far more reliable—such as the Friedman, the Fall's test, the Mazer, the Gilfillen and Gregg and many others. H.B.M.

Retreatment of the Pregnant Woman for Syphillis Following Penicillin

N. R. Ingraham, Jr. and associates (*American Journal of Obstetrics*, 56:340,

Aug. 1948) report a study of 52 women who had been treated for syphilis with penicillin before their pregnancy but were not treated during pregnancy. There were 3 abortions, one miscarriage, one stillbirth and one neonatal death, none of which could be attributed to spyhillis, and were probably due to other causes. There were 46 living infants, all apparently normal and with no evidence of syphilis. All but one of these infants was seronegative at birth, and this infant showed only 1 Kahn unit and became entirely seronegative "almost immediately." Serologic tests have remained negative, physical examination and roentgenograms of the bones have shown no evidence of syphilis. The follow-up period has been less than two months in 20 of these infants, and in these cases the diagnosis of normal is presumptive only; 6 infants have been followed up for two to six months; and 20 for six months or over; this latter group can be considered as definitely normal. Of the 52 women, 36 were seronegative at the time of delivery and 16 were seropositive. A study of the seropositive cases showed that duration of observation after treatment was more important in determining seronegativity than either the stage of syphilis when treatment was given or the dosage of penicillin within limits considered to be satisfactory. Of 10 mothers delivered more than two years after penicillin therapy, only one was seropositive; while of 11 mothers delivered within one year, 5 were seropositive; and of 35 delivered between one and two years after treatment, 10 were seropositive. If a woman has been treated for syphilis with penicillin with or without other drugs, and shows no recurrence of symptoms and either negative serology or a progressive fall in titer (using quantitative titered tests), retreatment during pregnancy may be considered unnecessary; but if there is any doubt as to the effectiveness of previous antisyphilitic therapy, the great effectiveness and relative safety of penicillin makes such retreatment desirable for the prevention of congenital syphilis in the infant.

COMMENT

The big problem underlying retreatment of syphilis during pregnancy when successful treatment has been carried out before pregnancy ensued is in establishing the criteria of cure. Penicillin has greatly simplified the treatment of syphilis during pregnancy and therefore there is no good reason why every such case of syphilis should not be treated. Of course, if the physician is in a position to have appropriate tests performed for the diagnosis of syphilis this should be done, since it is folly to treat the pregnant woman for syphilis if it is not present. When in doubt treat with penicillin and begin treatment as soon as the diagnosis of pregnancy is made. Large dosage is imperative. Look out for the baby immediately after birth and for several years following. Syphilis is very "elusive" but can be eliminated by a persevering doctor and a cooperating patient. ***H.B.M.***

GENERAL PRACTICE

—Concluded from page 135

of the cesareans done now are low cervicals.

Thank you once again for your comments and letter.

Charles E. Conner, M. D.
Cashmere, Wash.

Choose Your Chaos

In a letter to the *New York Times* in its issue of November 16, 1948, Dr. J. B. Pastore, Executor Director of the Hospital Council of Greater New York, evinced comical alarm concerning the concept that all qualified physicians should have the privilege of admitting their patients to all hospitals. He said that chaos would result if this were to occur.

It seems to us that there is quite a bit of chaos now—just about as much as there would be in the domain of the law if all qualified lawyers were not members of the bar and officers of the court, or if all qualified clergymen were not functioning as such in the church.

Medical BOOK NEWS

Edited by
ANDREW M. BABEY, M.D.

All books for review and communications concerning Book News should be addressed to the Editor of this department, 1313 Bedford Avenue, Brooklyn 16, N. Y. When books are sent to us with requests for review, selections for that purpose are promptly made.

FRANCIS GLISSON
1597–1677

Classical Quotations

● Certain swellings and knotty excrescences, about some of the joynts are observed in this affect; these are chiefly conspicuous in the Wrists, and somewhat less in the Ankles. The like Tumors also are in the tops of the Ribs where they are conjoyned with gristles in the Breast.

FRANCIS GLISSON
A Treatise of the Rickets. London 1668, p. 231.

Neurology

A Textbook of Clinical Neurology. With an Introduction to the History of Neurolgy. By Israel S. Wechsler, M.D. 6th Edition. Philadelphia, W. B. Saunders Co., [c. 1947]. 8vo. 829 pages, illustrated. Cloth, $8.50.

This is the sixth edition of a book that has established for itself an enviable position as a classic amongst textbooks. It is based mostly on personal teaching and clinical experience by an outstanding teacher who has had unusually rich material from which to draw upon for general conclusions. It is written in a facile and easily readable style, in language that is clear, concise and descriptive.

In this edition the chapter on psychometric tests has been completely rewritten and changed to psychological diagnosis of personality disorders in organic brain syndromes, and has again been written by Dr. David Wechsler, the author of the "Wechsler-Bellevue Intelligence Scale."

IRVING J. SANDS

Cancer

Entstehung und Fruherfassung des Portiokarsinoms. Weitere erfahrungen mit der Systematischen Kolposkopie an der Zurcher Fraunklinik. Zugleich ein Betrag zur Frage der Krebsentstehung. By Dr. Hansjakob Wespi. Basel, Switzerland, Benno Schwabe & Co., [c. 1946]. 8vo. 183 pages, illustrated. Cloth, 18 fr.

The origin and early recognition of cervical carcinoma is the subject of this book. The author recounts further experiences in the systematic use of the colposcope for the early diagnosis of cervical malignancy at the Zurich Gynecological Clinic.

Thus, studying the early changes occuring in the individual cells, he was led to propound his theory of the causation of cervical cancer. A chapter is devoted to this subject.

Included is a photograph of the colposcope used by the author, and where it can be obtained.

Appended is an extensive bibliography on the subject.

JACOB HALPERIN

Bacteriology

A Text-bok of Bacteriology. By R. W. Fairbrother, M. D. 5th Edition. New York, Grune & Stratton, [c. 1948]. 8vo. 480 pages, illustrated. Cloth, $6.00.

This book has run through five editions in eleven years. The material is presented in a clear and concise manner. However, in the opinion of this reviewer the subject matter is presented much too briefly for the needs of the medical student who depends on a textbook for a great deal of his information.

MORRIS L. RAKIETEN

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MEDICAL BOOK NEWS

—Continued from page 149

Protozoa

Laboratory Diagnosis of Protozoan Diseases. By Charles Franklin Craig, M.D. 2nd Edition. Philadelphia, Lea & Febiger, [c. 1948]. 8vo. 384 pages, illustrated. Cloth, $6.50.

The 2nd edition of Craig's *Laboratory Diagnosis of Protozoan Diseases* should need no introduction to workers in this field. The subject is thoroughly and masterfully treated and much new material has been added as the result of the World War. This edition is to be highly recommended both for reference and information for especial use regarding resident patients infected by protozoal diseases during military sojourn in the tropics.

MAX LEDERER

Psychiatry

The Clinical Application of Psychological Tests. Diagnostic Summaries and Case Studies. By Roy Schaefer, M.A. New York, International Universities Press, [c. 1948, The Author]. 8vo. 346 pages. Cloth, $6.75. (The Menninger Foundation Monograph Series No. 6.)

This volume by Roy Schafer M.A., is a textbook for students of psychiatry and psychology. Analysis of many cases of schizophrenia, depression and allied mental diseases are given in detail with the various psychological tests. This book is essentially for use in college studies.

ARTHUR D. JAQUES

Report on the Kinsey Report

Sex Habits of American Men. A Symposium on the Kinsey Report. Edited by Albert Deutsch. New York, Prentice-Hall, [c. 1948]. 8vo. 244 pages. Cloth, $3.00.

This is a broadminded critique of the celebrated Kinsey report by well known specialists interested in sex education, marriage, sociology, psychiatry and religion, with contributions by Mrs. Field and Mrs. Gruenberg.

It will be digested by nearly every person who has knowledge of its existence just as the Kinsey Report will be. The book is a challenge to a better understanding of the pedagogy of sex and emphasizes the gap between preachment and practice.

BERNARD SELIGMAN

Brain

Psychopathology and Education of the Brain-Injured Child. By Alfred A. Strauss & Laura E. Lehtinen. New York, Grune & Stratton, [c. 1947]. 8vo. 206 pages, illustrated. Cloth, $5.00.

The brain-injured child is at last receiving better methods of after-care and educational rehabilitation. A great deal of research on these unfortunates has resulted in getting the most out of these handicapped children.

The authors have tabulated some of the most practical diagnostic procedures in this little book.

THURMAN B. GIVAN

Allergy

Practice of Allergy. By Warren T. Vaughan, M.D. Revised by J. Harvey Black, M.D. 2nd Edition. St. Louis, C. V. Mosby Co., [c. 1948]. 4to. 1132 pages, illustrated. Cloth, $15.00.

In reviewing the first edition by the late Warren T. Vaughan, we remarked that it was an encyclopedia of allergy and should be in the library of everyone interested in allergy. Dr. Harvey Black has brought it up to date so that the above statement still holds. It is well written, stimulating to the imagination and at the same time factual. It can be highly recommended as the most exhaustive, reliable treatise on allergy.

GEORGE A. MERRILL

Heart Disease

Treatment of Heart Disease. By William A. Brams, M.D. Philadelphia, W. B. Saunders Co., [c. 1948]. 8vo. 195 pages, illustrated. Cloth, $3.50.

This volume is noteworthy especially for its practicality. The first chapter on the pharmacology is, in the opinion of this reviewer, the best. The discussion on the indications and action of medicaments used in cardiology is both basic and sound.

Perhaps the most serious criticism is found in the second chapter, "Treatment of Congestive Failure." The discussion of the importance of Low Sodium is definitely inadequate.

The many references to basic physiologic research on controversial subjects is to be commended. This book should be included in all hospital libraries.

HENRY D. FEARON

—Concluded from page 152

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MEDICAL BOOK NEWS

—Continued from page 150

History

Essays on Historical Medicine. By Bernard J. Ficarra, M.D. New York, Froben Pr., [c. 1948]. 8vo. 220 pages, illustrated. Cloth, $5.00.

These essays, in their progress down the centuries to the present day, present a wide choice of unusually interesting historical topics, for example, the autopsies on Saint Ignatius Loyola, Marcello Malpighi, Samuel Pepys, Napoleon Bonaparte, Abraham Lincoln. That on John Paul Jones is a remarkable recital because of the many definite findings one hundred and thirteen years after his death.

This selective collection of the author's publications in the current medical press has the merit for the busy doctor of affording fascinating glimpses of the great drama of medicine as played in momentous periods, each chapter being complete in itself. Take p.r.n.

ARTHUR C. JACOBSON

Streptomycin

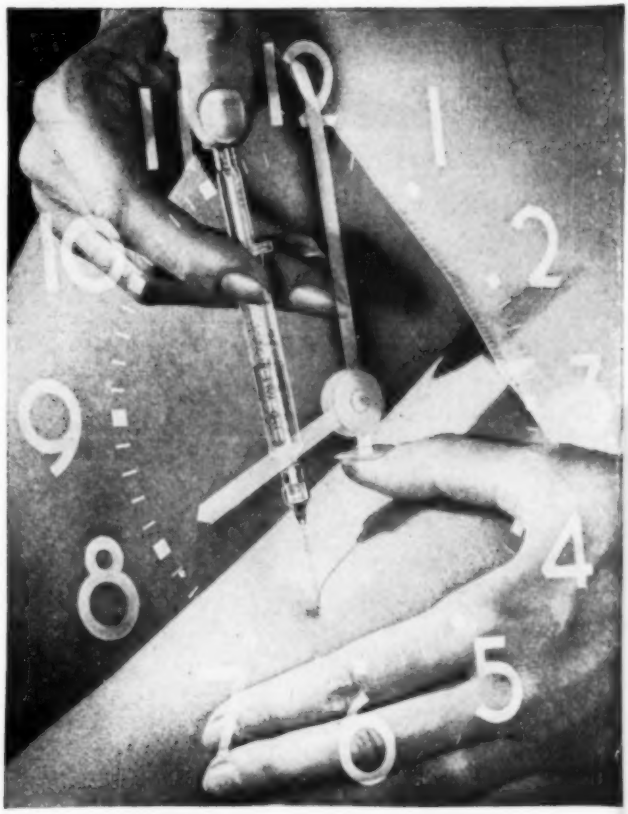
Streptomycin und Tuberkulose. Edited by Prof. G. Fanconi & Prof. W. Löffler, with contributions by Drs. J. Barth, M. Bosshard, Prof. O. Bucher, et al. Basel, Switzerland, Benno Schwabe (New York, Grune & Stratton), [1948]. 8vo. 357 pages, illustrated. Paper, 30 Sw.fr.

The book gives an excellent survey of our present knowledge about Streptomycin treatment of tuberculous diseases of the various organs. The introduction contains a list of absolute, relative, negative, and not yet determined indications for the Streptomycin treatment. More than twenty authors have written contributions, mostly in German, some in French. Each chapter has at its end a summary in English. The possibilities and limitations of intracavernous Streptomycin treatment are well described, ending in a definite statement, "that neither the sanatorium regime nor collapse therapy can be replaced by streptomycin." The book does not pretend to be complete or exhaustive, and it has not even an index, but nevertheless it is an important contribution to the literature on Streptomycin.

MAX G. BERLINER

—Continued on page 154

One-injection control of diabetes



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Gelatine U.S.P.

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MEDICAL BOOK NEWS

—Continued on page 152

Drugs

A Handbook of Commonly Used Drugs Including Certain Measures for the Control of Diseases Peculiar to the Tropics of the Western Hemisphere. By Michel Pijoan, M.D., & Clark Harvey Yeager, M.D. Springfield, Ill., Charles C. Thomas, 1947. 8vo. 198 pages, illustrated. Cloth, $3.75.

This is a brief review of the more important practical points on common drugs. It tells what they are, what they do, and how safely to use them. Since it is so brief, it will prove particularly useful as a quick reference book for physicians and students and nurses.

ANDREW BABEY

Surgery

Minor Surgery. By Frederick Christopher, M.D. 6th Edition. Philadelphia, W. B. Saunders Co., [c. 1948]. 8vo. 1058 pages, illustrated. Cloth, $12.00.

This book presents a wealth of minor surgical knowledge for office procedure and in the operating room.

It is well indexed and tabulated. References are grouped after each surgical procedure and presented and discussed for more detailed reference, for the reader's further investigation.

It is a book not only for the general surgeon's desk, but, also, for the surgical specialists and internes.

HUGH L. MURPHY

Pharmacology

A Manual of Pharmacology and its Applications to Therapeutics and Toxicology. By Torald Sollmann, M.D. 7th Edition. Philadelphia, W. B. Saunders Co., [c. 1948]. 4to. 1132 pages. Cloth, $11.50.

A heroic and fortunately successful effort has been made by the original author to revise this best of standard texts of pharmacology. The material of the previous editions has been greatly curtailed and all the new drugs have been added. The references are adequate and up to date. It is now printed in double columns but the practice of putting significant but not so important details in fine print has been continued. For the pharmacologist and the serious student this text is probably superior to all others.

JOSEPH R. DI PALMA

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REFERENCES:

1. J. Pediat. 32:1 (1948).
2. Am. J. M. Sc. 213:313 (1947).
3. J. Pediat. 32:119 (1948).
4. New England J. Med. 236:817 (1947).
5. New York State J. Med. 48:517 (1948).
6. Lancet 1:255 (1947).

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The synthetic hydrophilic colloid methylcellulose has a high degree of chemical uniformity which is frequently not found in natural gums. This is one of the advantages of the use of methylcellulose as a bulk laxative. According to Schweig in *N. Y. St. J. Med.* (48:1822 (1948)) the way in which the colloid takes up water makes it almost impossible to form an impaction. Methylcellulose forms a colloidal solution in any given amount in water, the viscosity varying from a soft smooth gel to a thin demulcent liquid. Duration of administration varied from 3 to 240 days in 37 patients under observation. No evidence of systemic changes or toxicity was observed in any of the patients who had had either chronic or acute constipation. Following use the stools passed were normal, soft and bulky and without accompanying griping, cramping or tenesmus.

Treatment of Menometrorrhagia

In a review of the problem of menometrorrhagia in the *J. A. M. A.* (135:557 (Nov. 1, 1947)) Fluhmann recommends the use of endocrine preparations to control the bleeding. Thyroid extract is of value in patients with low basal metabolic rates. Large doses of estrogens or progesterone are very effective in controlling the bleeding, but large doses must be employed. They may prove of curative value if used for a few days at the start of each bleeding period over several months. Estrone is given in daily doses of 20,000 units, estradiol dipropionate in doses of 2.5 mg., and estradiol benzoate in doses of 3.0 mg. Progesterone is administered intramuscularly in doses of 10 mg. each day for 4 or 5 days. Pregneninolone may be employed orally in doses of 40 to 50 mg. a day for 5 to 10 days.

—Continued on page 54a

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Gratifying Relief

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URINARY SYMPTOMS

Distressing symptoms of urinary tract infection such as urinary frequency, pain and burning on urination can be relieved promptly in a high percentage of patients through the simple procedure of administering Pyridium orally.

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MODERN THERAPEUTICS

—Continued from page 52a

Dimercaprol in Acute Iron Poisoning

Since there are occasions when unauthorized doses of iron salts, particularly among children, are taken, Edge and Somers made a study of the detoxifying effect of dimercaprol (BAL) on iron salts. It has been shown recently that large doses of soluble iron salts are toxic to test animals. In studies on mice, reported in *Quart. J. Pharm. and Pharmacol.* (21:364 (July-Sept. 1948)), the authors first determined the LD50 of dimercaprol alone when given orally and intravenously. Then they established safe doses to be used as the antidote against ferrous sulfate and ferric chloride. Control mice also received dimercaprol alone in the antidote dosage. Administration of BAL prior to large doses of the iron salts increased the toxicity of the iron salts when given intravenously. When given orally the BAL increased the toxicity if given after the iron salts but there was a slight protective action against ferrous sulfate when the BAL was given prior to the salt. Similar experiments with mercuric chloride verified previous findings that BAL increased the tolerance to the salt several fold. At least intravenously it appears that the toxicity is increased from the formation of a ferrous-dimercaprol complex. When ferrous sulfate and BAL were mixed in equal portions and the mixture injected the toxicity was greater than from an equal amount of ferrous sulfate alone. Thus the authors have shown that dimercaprol is not an effective antidote against toxic doses of iron salts.

—Continued on page 56a

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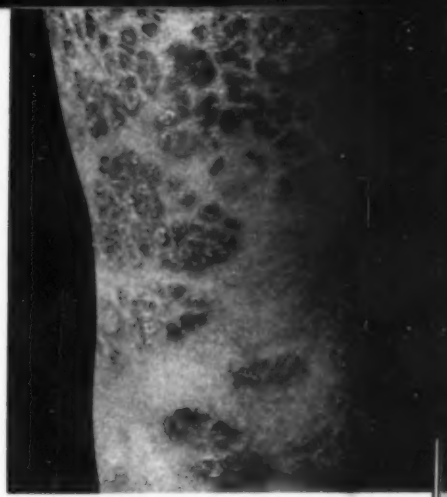
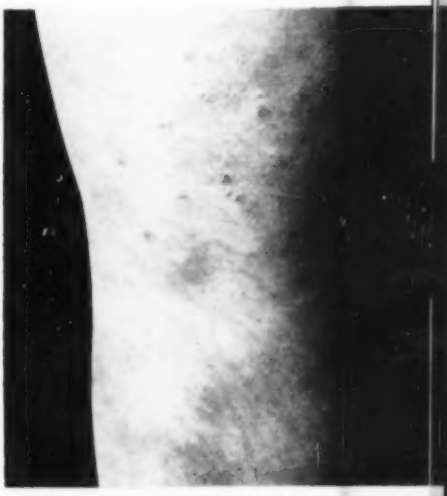


BEFORE USE OF RIASOL



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RIASOL for PSORIASIS

—Continued from page 54a

Antibacterial Effects of G-5, G-11, and A-151

In vitro, G-5 (2,2'-methylenebis (4,6-dichlorophenol)), G-11 (2,2'-methylenebis-(3,4,6-trichlorophenol)), and A-151 (a compound of 2-imidazolidinethione with silver nitrate) showed bacteriostatic action against various bacteria such as *Staphylococcus albus, Staph. aureus,* and *Escherichia coli.* However, in serial basin tests single scrubbings for 1 to 10 minutes with 2 or 6 per cent G-5, 2 per cent G-11, or 2 per cent A-151 did not reduce the bacterial flora of the hands and arms any more rapidly than ordinary soaps. The ordinary bacterial flora of the skin was reduced to about 5 per cent by the use of G-11 several times a day, and maintained at that level by continued use. However, no protection was given from subsequent contamination with other bacteria and there was no evidence of selective action against pathogenic bacteria, according to Price and Bonnett in *Surgery (24*:542 (Sept. 1948)). These compounds were also found to be very toxic to dogs when injected intravenously and, therefore, the authors conclude that they should not be used on wounds.

Podophyllin Used in Treatment of Condylomata Acuminata

Seventy-five cases of condylomata acuminata were treated with applications of 25 per cent podophyllin in compound benzoin tincture. Lesions were completely eradicated in all cases and only one application was required in 78 per cent. Only two cases required more than 3 applications. New and Marsh, writing in *U.S. Naval Med. Bull. (48*:831 (Nov.-Dec. 1948)) warn that repeated applications have a tendency to cause marked local sensitivity. Compound benzoin tincture was selected as the vehicle because the alcohol content keeps the podophyllin in solution while

—Continued on page 58a

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It is therapeutically reliable, does not disturb the gastric function, depress the circulatory system or habituate the patient to its use.

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Mail this ad with your Rx blank for a generous trial supply.

for effective bowel management

MODERN THERAPEUTICS

—Continued from page 56a

the benzoin, storax, aloe, and tolu causes the preparation to adhere to the surfaces to which it is applied. Podophyllin apparently acts directly on the epithelial cells.

Chloromycetin in Scrub Typhus

Smadel *et al* have reported the beneficial effects observed in the treatment of 25 cases of proven scrub typhus with the antibiotic chloromycetin, in *Science (108*:-160 (Aug. 13, 1948)). The patients received an initial dose of 50 mg. per Kg. of body weight with doses of 200 to 300 mg. every 2 to 4 hours thereafter. Treatment was continued until at least the 12th day after onset of the disease, at first, but this time was reduced until the last 7 patients received the drug for only 24 hours, with a total dosage of about 6 Gm. The shorter regime brought about responses equal to those from the longer regime. Fever returned to normal within 10 to 96 hours following institution of therapy. The febrile days following the onset of the disease averaged 7.5 in the treated group in contrast to 18.1 days in a control group of 12 patients. The average hospital stay was 19.2 days for those in the treated group and 30.7 for those in the untreated control group. There were no toxic reactions, no complications and no deaths in the treated group as compared with two complications and one death in the control group.

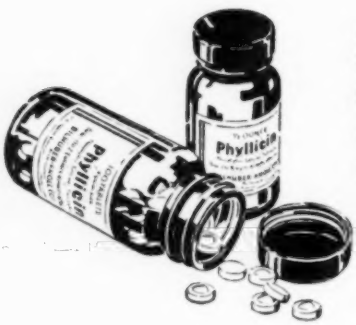
Hexachlorocyclohexane, A New Potent Scabicide

The new scabicide, 1,2,3,4-5,6-hexachlorocyclohexane, was used in the treatment of 100 unselected cases of scabies. The gamma isomer of 1,2,3,4,5,6-hexachlorocyclohexane was incorporated in a vanishing cream base to the extent of 1 per cent.

—Concluded on page 60a

For the Failing Heart

Phyllicin



A "theophylline" for oral administration in cardiac diseases - quick acting and well tolerated. Phyllicin is a potent diuretic and myocardial stimulant, useful for the relief of cardiac distress and pain, to diminish dyspnoea and to reduce edema.

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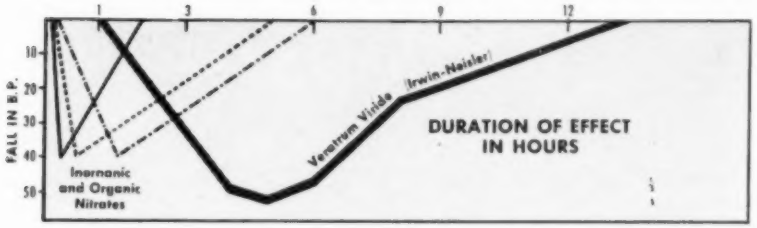

Veratrite affects a marked relief of headache, palpitation and dizziness in hypertensive subjects, together with a feeling of well-being in the majority of cases of less-than-severe degree.

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Each tabule contains: veratrum viride (bio-assayed) 3 Craw Units; sodium nitrite 1 grain; phenobarbital ¼ grain.

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Upon the occasion of the thirtieth anniversary of the successful formulation of Occy-Crystine by a practicing physician, the makers of this product pause to convey their appreciation to the many members of the profession—who, by their numerous prescriptions and voluntary communications over the past three decades, have testified to its therapeutic efficacy and to the beneficial results derived from personal and clinical use.

During the years ahead, with the help and guidance of leaders in the pharmaceutical, biochemical and physiological fields, and in the light of ever newer knowledge, we shall continue to keep reports on Occy-Crystine therapy fully abreast of the latest findings on the value of this saline cathartic, cholagogue, diuretic and sulfur-bearing agent.

C. F. Burnett M.D.

MEDICAL DIRECTOR

1918 ~ 1948 ~ ~ 30 YEARS YOUNG

MODERN THERAPEUTICS

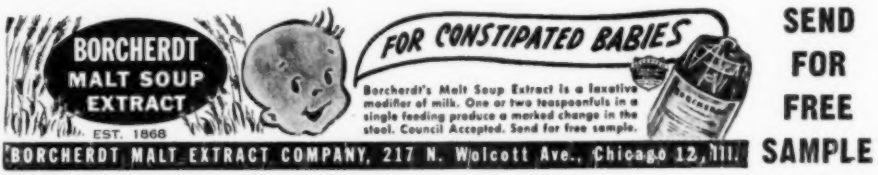
—Concluded from page 58a

Without preliminary bathing a thin film of the cream was rubbed into the entire cutaneous surface. About 15 to 25 Gm. were required for one adult treatment. The patient was not to bathe for 24 hours. After a thorough bath all underclothing, night clothes and bed linen were to be changed and thoroughly laundered. After one week the patient was then examined, as this allowed ample time for any ova to hatch. There was 100 per cent cure in these patients. Sixty-one received but one treatment, 36 received 2 treatments and 3 received 3 treatments. There was complete relief of pruritis within 24 to 48 hours and relief of itching in many cases within 2 or 3 hours. This remedy was found to be effective in cases in which other remedies had failed. There were no cases of irritation or sensitivity recorded and there were no contraindications even in the presence of severe dermatitis from scratching.

This drug has also proven to be effective in the control of chiggers, ticks, fleas, cockroaches, bedbugs, and pediculi capitis, corporis and pubis.

The toxicity of the drug is quite low when applied to the skin or even when administered orally, according to tests on experimental animals.

According to Cannon and McRae in *J. A.M.A.* (*138*:537 (Oct. 23, 1948)) all patch tests performed one to two months after cure to determine the possible development of sensitivity were negative.



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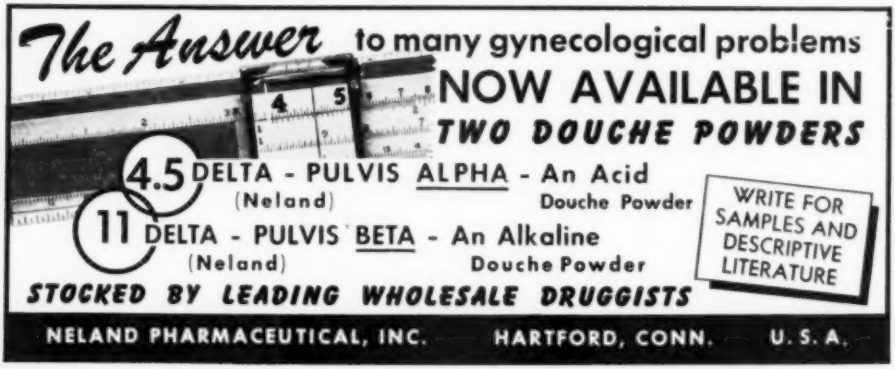

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NEWS AND NOTES

Schering President Lauds University Research

Although there are approximately 2,500 industrial research laboratories in the United States today, it has been estimated that more than 95 per cent of the modern chemical industry is based directly on university research, Francis C. Brown, president, The Schering Corporation, Bloomfield, N. J., recently told a group of New York physicians.

Calling for a closer cooperation between industry and universities on research activities, Mr. Brown said that industry must be liberal in providing funds and facilities in order to attract better research workers. "There can be no doubt," he said, "but that the universities which have contributed so much to science in the past will make even greater contributions in the future."

He pointed out that all too often industrial management puts time limits on research projects which mitigate against success, and also cuts business expenses to the detriment of its research activities, rather than other phases of management. Whenever industry contributes money to support university or non-profit institutional research projects, the government indirectly foots a substantial part of the bill anyway, he said, because such expenditures ordinarily are deductible for tax purposes, and thus reduce the base upon which income and profit taxes are collected.

Praising the research facilities planned for the New York University-Bellevue Medical Center, which will be built on New York's East Side, within a few blocks of the site of the United Nations, Mr. Brown pointed out that medical research has fought a long, tough, successful battle for funds to carry on its work. Until the present century, industry did virtually nothing either directly or indirectly to support university research, he added.

"I am especially interested in your program for future research because I am an executive of a pharmaceutical company," he continued. "I am fully satisfied that the growth and future development of our company will be stimulated far more by the work which will be done in other research minded medical institutions, than by the combined effort of the industrial re-

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Tarss, J. M.: M. Times 77:101 (April) 1949.

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Astringent • Hemostatic • Analgesic
Antipruritic • Antiseptic

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Send Sprace samples for clinical trial.

☐ Ointment ☐ Suppositories

Dr. _____

search workers for all of the pharmaceutical companies.

"Therefore, I have a vital interest in seeing your plans materialize into buildings, equipment, and moving reality. When your new medical center shall be completed, we shall be prepared to work with you and help you, and I am sure that others in the pharmaceutical industry will gladly do likewise."

Grant For Research In Chemistry of Nutrition

Dr. Detlev W. Bronk, President of The Johns Hopkins University, announced, recently, that The Robert Gould Research Foundation, Cincinnati, has made a grant-in-aid of five thousand ($5,000.00) dollars for research in 1949 by Dr. E. V. McCollum, Professor Emeritus of Biochemistry at the School of Hygiene and Public Health of the University.

The fund will enable Dr. McCollum, the discoverer of Vitamins A and D and one of the discoverers of Vitamin B_1, to continue his experiments in the chemistry of nutrition, studying a problem which has challenged the efforts of chemists for fifty years, namely, the separation in pure form of amino acids which form the digestion products of proteins in the body.

At present, only six of the twenty-three known amino acids can be separated from the digestion mixture with a reasonable expenditure of time and effort. Amino acids are the end products of digested meat, eggs and other proteins in the intestines. Under the terms of the grant of The Robert Gould Research Foundation, Dr. McCollum will seek to make available for use the remaining amino acids which are today rare and costly chemicals.

Pure amino acids are much needed in medicine and surgery, for intravenous feeding, the treatment of gastric ulcer, and other specific purposes in nutritional therapy as well as by investigators conducting experiments in the basic sciences

—Concluded on page 64a

. . . to relieve the strain of

CHRONIC IRREGULARITY

WHEN aberrations of the menses suggest that normal function has overstepped the bounds of physiologic limits—the physician is often confronted with a condition which proves highly distressing to the patient. For such cases (as in amenorrhea, dysmenorrhea, menorrhagia and metrorrhagia), many physicians rely on Ergoapiol (Smith) with Savin as the product of choice. By its unique inclusion of all the alkaloids of ergot (prepared by hydroalcoholic extraction), and the presence of apiol and oil of savin—Ergoapiol (Smith) with Savin provides a balanced and sustained tonic action on the uterus, affording welcome relief in many functional catamenial disturbances. It produces a desirable hyperemia of the pelvic organs, stimulates smooth, rhythmic uterine contractions, and also serves as an efficient hemostatic and oxytocic agent. General dosage: 1 to 2 capsules 3 to 4 times daily.

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NEWS AND NOTES

—Concluded from page 63a

of biology, biochemistry, physiology and bacteriology.

It is stated that novel procedures developed by Dr. McCollum since 1944 make it practicable to produce on a generous scale two of the rate amino acids, histidine and lysine, this method requiring half a day in contrast to the one month of the old method.

Barbiturates Leading Cause of Fatal Poisoning

Fewer accidental deaths have been recorded in recent years from virtually every type of poison-containing compound, with the notable exception of the barbiturates, which are now by far the leading cause of fatal accidental poisonings, according to the Statistical Bulletin of the Metropolitan Life Insurance Company.

In 1946 barbituric acid and its derivatives accounted for more than a quarter of all fatal accidental poisoning in the United States.

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Your women patients will welcome the prompt relief from pain and distress when you prescribe

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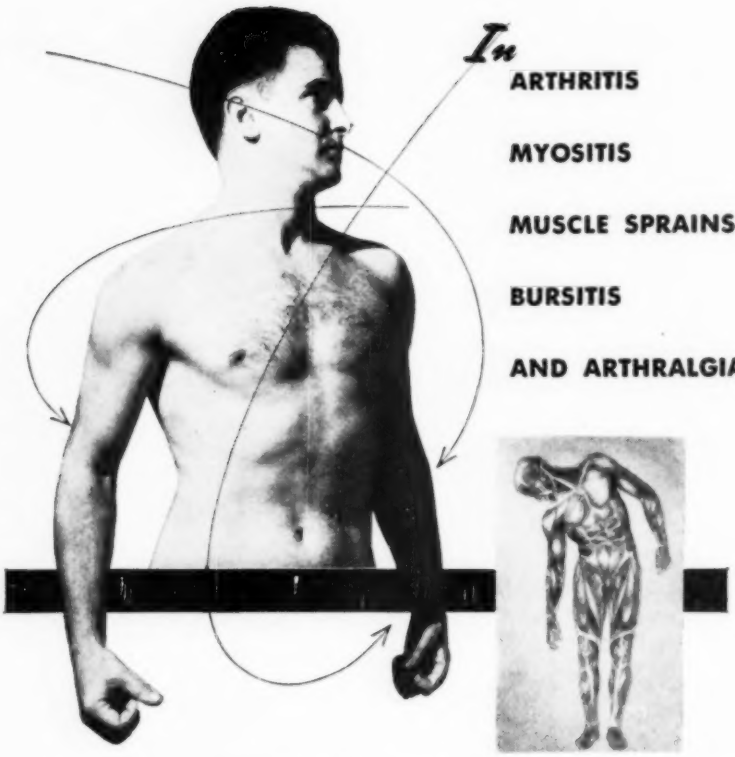

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Percutaneous absorption of methyl salicylate not only reinforces the topical effects of Baume Bengué but can enhance other systemic measures used to combat the underlying disease processes. The proof of the systemic effects of such preparations was established by the fundamental work of Moncorps, Kionka, Hanzlik, Brown and Scott.

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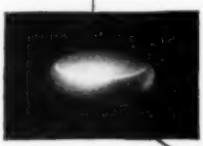
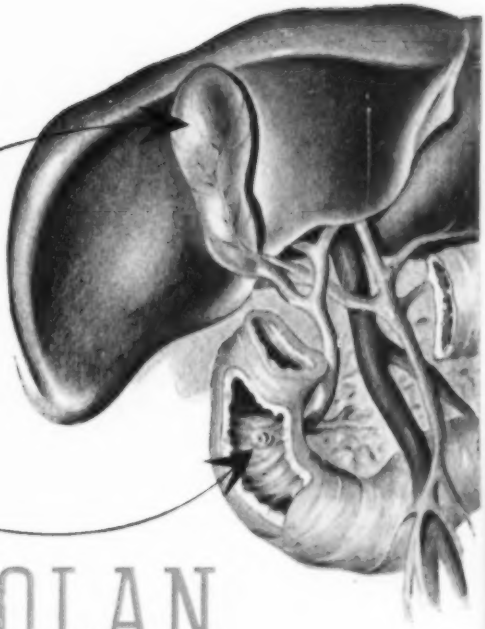
a complete gallbladder drug regimen in a single tablet





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FOR NONCALCULOUS BILIARY-TRACT STASIS

Formula: Each tablet of Neocholan contains:

Dehydrocholic Acid Comp., P.-M. Co.	265 mg. (4 grs.)
Dehydrocholic Acid	250 mg. (3 3/4 grs.)
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Rationale: Neocholan exerts two distinct actions:

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2 . . . Sphincter Relaxation—homatropine methylbromide and phenobarbital combine to assure sphincter relaxation so that the bile may discharge freely into the duodenum.

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For increased efficiency, ease of administration and economy—

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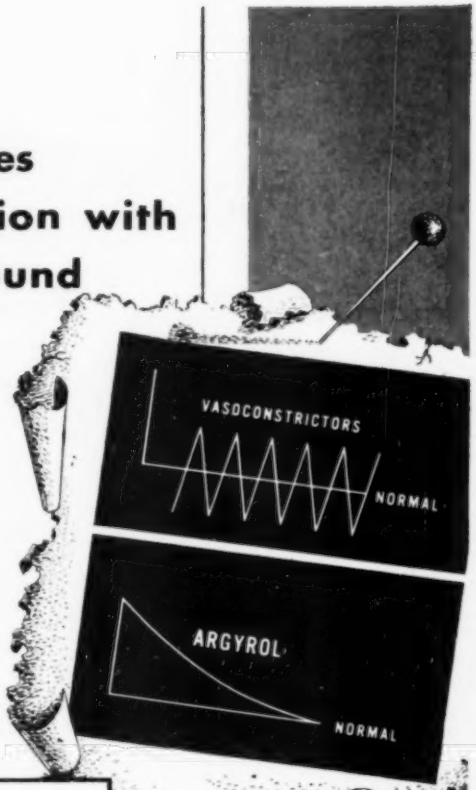

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